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TROPICAL DISEASES BULLETIN

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BUREAU OF HYGIENE AND TROPICAL DISEASES

TROPICAL DISEASES BULLETIN

Vol. 45] 1948 [No. 6

SUMMARY OF RECENT ABSTRACTS*

V. LEISHMANIASIS

VISCERAL LEISHMANIASIS

Epidemiology: Aetiology: Transmission

FALCÓN TREJO (p. 984) reports kala azar from Badajoz, Spain.

An account of leishmaniasis in Greece is given by MALAMOS (p. 1), who considers the geographical distribution of kala azar (here a disease of infants), canine leishmaniasis (due to *L. donovani*), and oriental sore. The chief vector of kala azar in Greece is *Phlebotomus major*, and of oriental sore *P. sergenti*; only occasionally is *P. papatasi* involved.

HO *et al.* (p. 987) have found visceral leishmaniasis in dogs in part of China where kala azar is present. Leishmania were found in the skin of most of the infected dogs.

SHIH LU CHANG (p. 1055) describes two media, one semi-solid, the other fluid with a solid base, for cultivation of leishmania and *T. cruzi*. Both give better growth than the media usually employed. For details the original should be consulted. With the solid-base medium, SHI LU CHANG and NEGHERBON (p. 1056) have studied the growth characteristics of various species of leishmania, and of *T. cruzi*, but for details the original should be consulted.

PEREIRA and MEDINA (p. 188) describe a method of staining leishmania, especially in tissues.

ADLER (p. 983) has observed the behaviour of a Sudan strain of *L. donovani* in *P. papatasi*; the infection rate was low in sandflies fed on a diseased hamster. The infection rate provides one means of differentiating strains of *L. donovani*. Differentiation of the various species of *Leishmania* may be determined by consideration of results of cultivation experiments, infection of hamsters and of sandflies. For details the original should be consulted.

DE AZEVEDO and TEIXEIRA (p. 981) note the various species of *Phlebotomus* found in Lisbon in summer and autumn, and their habitats and blood preferences. Only 2 per cent. showed positive precipitin tests with anti-human sera, whereas 22·5 per cent. were positive with anti-bovine serum.

DOLMATOVA (p. 982) has studied the sandflies of a district in the Caucasus. In this area there are numerous burrows, some occupied by birds, and the

*The information from which this series of summaries has been compiled is given in the abstracts which have appeared in the *Tropical Diseases Bulletin*, 1947, v. 44. References to the abstracts are given under the names of the authors quoted, and the pages on which the abstracts are printed.

sandflies breed in these burrows. Several species known elsewhere to transmit kala azar occur here; the author thinks that *P. perniciosus* var. *tobbi*, is probably a natural vector of *L. donovani*, as it can be infected experimentally, and attacks man.

SHORTT (p. 511) has answered the criticisms previously made by MALONE and BROOKS [this *Bulletin*, 1945, v. 42, 357] on the experimental work done on the transmission of kala azar by *Phlebotomus argentipes*. FENG and CHUNG (p. 1055) report (for the first time) successful transmission of kala azar from dog to hamsters by the bite of *P. chinensis*, and also that hamsters became infected when inoculated with flagellates from *P. sergenti* var. *mongolensis* previously fed on an infected dog.

Diagnosis: Clinical Findings

DE AZEVEDO (p. 984) writing from Portugal, notes that the various standard methods of diagnosis of kala azar may give negative results, and advocates examination of material from the nose, for leishmania. With a platinum loop the mucous membrane is scraped until the surface is broken; in 11 cases examined, 9 were positive. The procedure is simple, but it is necessary to break the surface since the organisms are in the histiocytes of the submucosa.

The cephalin-cholesterol flocculation test was found by MAKARI (p. 298) to be strongly positive in eight cases of infantile kala azar.

DHARMENDRA *et al.* (p. 189) have prepared an antigen from Kedrowsky's acid-fast bacillus, to be used in a complement-fixation test for kala azar.

ADLER (p. 983) shows that in leishmaniasis there is proliferation of the reticulo-endothelial cells and also a secondary round-cell infiltration; he thinks that the latter reaction is a curative one, and that lymphocytes play some part in defence. This reaction is marked in dogs (in which the disease is usually chronic), but is slight in spermophils (in which the disease is acute and fatal).

PARRINELLO (p. 297) reports on the condition of the blood in infantile kala azar in Italy.

FELDMAN (p. 297) describes kala azar in a British soldier who had served in the Mediterranean; the disease developed 4 months after return to England. NORMAN (p. 54) mentions a case of long latent period in kala azar.

DEBONO (p. 985) states that in Malta, kala azar is a disease of young children rather than of infants. He describes the incubation period, onset and course of the disease, and the means he uses for diagnosis and treatment. It responds well to intravenous antimony.

Treatment

VAN DYKE and GELLHORN (p. 512) have tested in hamsters 188 new compounds for activity against the Sudan strain of *L. donovani*, but none has proved better than the recognized drugs.

The same authors (p. 298), noting that pentavalent antimony compounds are more effective, and less toxic, than trivalent compounds in leishmaniasis, describe investigations to find if there is a correlation between therapeutic activity of a drug and the amount of antimony present in liver and spleen of treated animals. The results were essentially negative in that the presence of high concentrations of the drugs (pentavalent compounds) was not synonymous with activity.

KIRK (p. 986) reviews the treatment of kala azar in the Sudan, where the use of antimony effects cure in 70 per cent. of cases, which would almost all be fatal without it. Use of the diamidines has further improved the results of treatment. The appearance of dermal lesions during or after treatment is of good prognostic significance; they may persist 20 years or more without affecting health.

KIRK and SATI (p. 885) in the Sudan report favourably on the results achieved in kala azar with sodium antimony gluconate [sodium stibogluconate] given intravenously in concentrated solution, for 6–10 injections, over a short period (as short as 6 days in some cases). The results in a small series were better than when the drug was given in smaller doses over a longer period, and the brevity of the course is in itself an advantage. MAEGRAITH *et al.* (p. 886) treated eight patients with kala azar (Indian or Mediterranean strains) with sodium stibogluconate, with one death and seven cures. The drug was given intravenously, once or twice daily for 10 days, and severe reactions occurred in five patients, and were attributed to it. In the fatal case there was shock and circulatory failure after the last dose, but the actual cause of this could not be ascertained at post mortem examination there was no evidence of accumulation or anaphylaxis, nor was it due to a defective batch of the drug. Cure was confirmed parasitologically, sometimes 3–4 months later. CHOUDHURI (p. 298) reports cure in 22 of 23 patients with kala azar (in India) treated with sodium antimony gluconate (Stibatin).

SARROUY *et al.* (p. 55) have used a new antimony preparation (antimoniate of N-methylglucamine) in the treatment of a child with kala azar; it was successful, but the dosage has not yet been determined, though the preparation is said to be only half as toxic as Pentastib. DURAND *et al.* (p. 56) report further use of this drug, confirming its value and low toxicity. It is rapidly excreted by the kidneys. They treated 6 cases with very good results, though sufficient time has not yet elapsed to decide if permanent cure has been obtained. SARROUY *et al.* (p. 807) report three more cases successfully treated with this drug, which they regard as the most efficacious yet discovered.

The antimony content of different batches of urea stibamine varies, and the drug is not a compound of uniform formula. BOSE *et al.* (p. 189) have worked out the toxic dose for mice, but there is considerable variation. Assay of the drug must still be made biologically, since the relation of antimony content to toxicity is not known, and there is no indication which fraction is therapeutically active. To avoid the toxic symptoms which often arise as a result of treatment with urea stibamine, Ho (p. 189) in China gives relatively small doses for kala azar, and has found that with these, given once or twice each week, most cases are cured.

HARRISON and FULTON (p. 190) describe the changes which take place in the spleen of *Cricetus auratus* on infection with *L. donovani*, and show that although the enlarged spleen diminishes in size on treatment with 2-hydroxy stilbamidine, there is always a residual splenomegaly, even after cure. FULTON and DUNITZ (p. 988) discuss the constitution of the toxic substance created when stilbamidine is irradiated. SALTZMAN (p. 988) describes a method for estimation of stilbamidine in urine and blood, but FULTON, in comment, criticizes the technique employed.

ADLER and TCHERNOMORETZ (p. 406) have failed to cure dogs, naturally infected with *L. infantum*, with stilbamidine or neostibosan. There is always a residual skin and gland infection, even after intensive treatment, and the authors therefore advise that as such dogs serve as a reservoir for disease in man, they should be removed from endemic centres or destroyed.

CUTANEOUS AND MUCO-CUTANEOUS LEISHMANIASIS

STEINHAUER (p. 987) describes the recurrent form of cutaneous leishmaniasis which is common in Palestine. This form simulates lupus vulgaris, and leishmania are difficult to demonstrate except by cultural methods. The intradermal leishmania vaccine reaction is positive in 97 per cent. of cases, and biopsy shows characteristic tuberculoid structure. He reports a case of a

verrucose form of this disease, which, though common in South America, is rare in the Middle East.

PIERS (p. 889) reports a case of muco-cutaneous leishmaniasis from central Kenya, and notes a few cases of kala azar from the same area. This is the first time that cases have been reported from this place, and it is not known whether a focus existed before, or whether the disease has been introduced as a result of troop movements from Abyssinia. Penicillin treatment produced some improvement in the muco-cutaneous lesions.

ANSARI (p. 191) uses penicillin to control bacterial infection when isolating *L. tropica* in culture. He adds 1,250 units to each cubic centimetre of N.N.N. medium.

ANSARI (p. 887) describes a substance in commercial preparations of vitamin B, which stimulates growth of *L. tropica* in culture, and another which inhibits it. The former is heat-labile, the latter heat-stable.

JERACE (p. 808) has found *P. perfiliewi* in the Abruzzi area of Italy, where it is the vector of oriental sore.

Working in Calabria, TIMPANO (p. 299) claims to have transmitted oriental sore from man to man, three times by mosquitoes and once by sandflies. The insects (and houseflies) were allowed to feed on sores, and were then transferred to healthy persons, on whom they fed. He also claims to have found flagellates in the pharynx and stomach of two mosquitoes and a sandfly. In comment, WENYON remarks that the arrangement of the experiments seemed to favour mechanical transmission rather than development of leishmania in the flies, and comments on the shortness of the incubation period (12–15 days).

DOLMATOVA (p. 887) has made observations on the biology of *P. papatasi*, *P. sergenti* and other sandflies in a focus of oriental sore in Tadjikistan. They have, apparently, no food preferences, but feed on the most accessible animals.

KERVRAN (p. 190) states that *P. roubaudi* is probably the common transmitter of cutaneous leishmaniasis in the French Sudan.

The histo-pathological processes involved in the invasion of the tissues of mice by *L. tropica* have been described by LEVINSON and SKADOVSKAJA (p. 888), and details should be sought in the original abstract. The infection was initiated by inoculation of *L. tropica* from the moist type of human oriental sore.

DOSTROVSKY and SAGHER (p. 1056) have found, in a number of trials, that the culture method of diagnosis in oriental sore gives more positive results than examination of smears for leishmania, particularly in old, chronic cases, in which the lesions may resemble those of lupus or syphilis. SAGHER (p. 889) has used a vaccine of *L. tropica*, in graded dilutions, for skin tests in cases of oriental sore of various types. He concludes that in the recurrent type (with infection lasting more than one year) there is a more pronounced allergic component than in the nodular form (with infection of less than one year). DOSTROVSKY and SAGHER (p. 987) have found the intracutaneous test (with the vaccine prepared by the former) positive in most cases of oriental sore (either nodular or recurrent) tested in the Jerusalem area, whereas examination of the lesions for parasites was negative in more than half of the cases. The chances of non-specific reactions are small.

ROMAÑA *et al.* (p. 300) have found a focus of cutaneous leishmaniasis in Tucumán, Argentina.

PESSÔA and BARRETTO (p. 300) summarize the evidence that American cutaneous leishmaniasis is most common in men whose work takes them into forests, where sandflies abound. *Charles Wilcocks*

RABIES

UNGARI, C. Meningoencefalomielite da virus rabico a decorso clinico anomalo. **[Meningo-encephalitis due to Rabies Virus, having an Atypical Clinical Course.]** *Pediatria.* 1943, Feb., v. 51, No. 2, 52–8.

The author refers to the difficulties experienced in deciding, when an acute ascending paralysis of the Landry type occurs at the end of or shortly after completion of anti-rabies treatment, whether it is a latent encephalomyelitis activated during the treatment, a paralytic accident of vaccine treatment or a case of rabies caused by street virus or fixed virus modified by vaccination.

A case of street virus infection which followed an atypical course is described :

A girl aged 7 years was bitten on the face by a stray dog, later confirmed by biological tests as having been rabid. Local disinfection was effected and anti-tetanus serum given within a few minutes ; intensive anti-rabies treatment was commenced with PUNTONI's phenolized vaccine within 48 hours. On the 21st day of treatment (23 days from the date of bite), the child suddenly developed high fever, followed two days later by signs of a paralysis which ascended from the lower limbs to the cranial nerves before death supervened on the 9th day of illness.

The main symptoms were those of paralysis with fairly well marked meningeal signs, itching in the bite scar and changes in the mental state (agitation, hallucinations, delirium). At no time was there hydrophobia or aerophobia, deglutition remaining comparatively unimpaired until death.

Histological examination of the brain revealed no Negri bodies, but the so-called Babes nodules were found in the superior olivary body.

Biological tests made on two guineapigs by the inoculation of bulbar material resulted in the death of the animals on the 18th day, with the presence of numerous and typical Negri bodies in the horn of Ammon. A second and third passage resulted in death of the test guineapigs on the 11th and on the 7th days respectively, with similar post mortem recovery of Negri bodies. The diagnosis of street virus was therefore established.

The difficulties of establishing a differential diagnosis on clinical grounds alone are discussed. *G. Stuart*

CAMPBELL, T. C. & DEFRIES, R. D. **Some Observations on the Preparation of Rabies Vaccine using Phenol.** [Abstract.] *Canadian J. Pub. Health.* 1948, Feb., v. 39, No. 2, 82.

" The introduction of the mouse test by Webster in 1939 made possible the determination of the antigenicity of rabies vaccines. As a result, vaccines of greater antigenic value have been prepared. A modification of the method of preparing rabies vaccine employing phenol (Semple method) is described in which phenol, 1 per cent, is added to a 30 per cent suspension of rabid brain tissue, in place of an 8 per cent suspension as usually employed in the preparation of rabies vaccine by the Semple method. The antigenic value of the vaccines so prepared has exceeded the minimum standard as recently established by the National Institute of Health, Washington, namely protection against 1,000 M.L.D. of challenge virus. A change, also, in the strain of virus in the preparation of both human and veterinary vaccines may be a contributing factor to their improved antigenicity. Vaccines for veterinary use prepared from rabid calf brain tissue possess a much greater antigenic value than vaccines made from rabbit brain tissue. Observations over a period of years of veterinary vaccines prepared from calf brain and processed by this method indicate that their potency is retained for a much longer period than that of

vaccines prepared by the standard Semple method for human use. The destructive action of freezing on rabies vaccines containing phenol is known. Further supporting evidence of this fact is supplied."

HABEL, K. & WRIGHT, J. T. **Some Factors influencing the Mouse Potency Test for Rabies Vaccine.** *Pub. Health Rep.* Wash. 1948, Jan. 9, v. 63, No. 2, 44–55, 3 figs.

A mouse test for the potency titration of rabies vaccine was first described by HABEL in 1940, since when official recognition has ensured its routine adoption as the basis of a minimal potency requirement of all rabies vaccines produced in the U.S.A. for human or veterinary use.

Variations in the results of the test have, however, been observed by workers in different laboratories and it was in order to determine the factors responsible for such variations and, if possible, to eliminate them that the study described in this paper was undertaken.

In this connexion the influence of (*a*) technician, (*b*) strain of mice and (*c*) strain of test virus was closely investigated, with the result that in (*b*) and in (*c*) probable explanation was found.

Thus as regards (*b*) it emerged that, with the technique employed in the standard test, strains of mice at the age of 4 weeks may vary in their ability to be immunized with a particular rabies virus. As regards (*c*) it was shown that a wide variation of "invasiveness" (*i.e.*, the ability to cause rabies in immunized mice) exists among fixed viruses even if, as in the present study, substrains of the original Paris (Pasteur) fixed virus are used. The substrains in question had been carried in different laboratories over a period of years by different individuals using different intracerebral passage techniques; any differences in their present characteristics must, therefore, have occurred through repeated animal passages over a long period of time.

In the light of the above findings, the authors consider it necessary to standardize the technique of the test and in this sense detail requirements for an acceptable determination of potency.

Of these requirements, reference need only be made here to: (*a*) type of test mouse and (*b*) the standard test virus.

(*a*) Type of test mouse.—The test is based on the use of white Swiss mice of either sex, approximately four weeks old, uniform in weight (11–13 gm.).

(*b*) The standard test virus.—A standard test virus will be supplied by the National Institute of Health, preferably only on request at approximately yearly intervals. [The use of such a standard virus will largely eliminate virus variations from routine potency testing. A standard virus may be obtained from pooled frozen virus which, as has been shown, will retain its titre for at least 10 months, with relatively slight variation in the titration end-points from test to test. Further to reduce the possibility of a standard virus changing its characteristics because of animal passage in different laboratories, the number of passages of the reference standard test virus actually used in determinations of potency should be held to a minimum.] *G. Stuart*

AMERICAN J. PUB. HEALTH. 1948, Jan., v. 38, No. 1, Pt. 1, 97–9. **Recommended Methods for Rabies Control.** Adopted by the Committee on Research and Standards, October 6, 1947, American Public Health Association.

A Conference on Rabies held in April, 1947, at the University of Pennsylvania reached complete agreement on the means whereby rabies control, undertaken on a national basis, could best be effected in the U.S.A.

The following paragraphs summarize the principal recommendations :

1. Active cooperation on the part of the Federal Government :
   (*a*) by contributing funds and personnel to affected States ;
   (*b*) by establishing a central bureau for the collection from and distribution to States, agencies and individuals concerned in the control programme, all information on the incidence among animal species and on the place of occurrence of rabies.

2. Prime consideration should be given to : (*a*) adequate diagnostic facilities; (*b*) the control of animals capable of transmitting the disease ; and (*c*) mass immunization of susceptible animals, particularly dogs.

(*a*) and (*b*) need no comment ; they conform to orthodox procedure.

As regards (*c*) : it is held that the vaccination of dogs, combined with other control measures, provides the most satisfactory method for the prompt control of rabies. Evidence shows that a single 5 ml. subcutaneous injection of an accepted canine rabies vaccine is effective in a mass vaccination campaign, but that the administration of three doses of such vaccine in 5 ml. amounts, one week apart, affords greater immunization. To secure permanent reduction in the number of susceptible dogs, annual immunization is advocated.

Vaccinated dogs, identifiable as such by suitable tags, may be allowed at large 30 days after vaccination. Finally, the need is emphasized for a comprehensive educational programme to bring the subject of rabies and its control before the public. *G. Stuart*

KORNS, R. F. & ZEISSIG, A. **Dog, Fox, and Cattle Rabies in New York State Evaluation of Vaccination in Dogs.** *Amer. J. Pub. Health.* 1948, Jan. v. 38, No. 1, Pt. 1, 50–65, 11 figs.

This article describes an epizootic of rabies continuing since 1943 in New York State and details measures for its control among the animal species affected there.

1. *Incidence.*—The epizootic has been characterized by the introduction and spread of the virus among foxes and cattle, with a concurrent sharp decline in canine rabies—a decrease ascribed in large measure to the extensive practice of dog vaccination. Thus in 1946, rabies was reported in 377 dogs, 308 foxes and 440 cows ; during the first nine months of 1947, it was reported in only 40 dogs, but in 218 foxes and 173 cows. Rabies in cattle seems clearly to have been due to the bites of rabid foxes ; fox rabies, with, as corollary, cattle rabies, has spread in a slow radial fashion over a period of two years.

2. *Control Measures.*—(*a*) Control of the dog problem.—Following on the acceptance of the HABEL rabies vaccine potency test and on the demonstrated value of approved anti-rabies vaccines in canine prophylaxis, a further measure of control has been added to that previously in force, *viz.*, restriction of the activity of dogs in areas where rabies was certified by the State Commissioner of Health to be present.

To be effective, mass vaccination of dogs presupposes immunization, spread over an area at least county-wide, of not less than 70 per cent. of the enumerated dog population ; it should be carried out in as short a period as possible, preferably within a month, so that the majority of the dogs in the area will attain maximum levels of immunity about the same time. When this percentage is achieved, the Commissioner of Health may designate " certified areas " (*i.e.*, where rabies exists) as areas in which vaccinated dogs may be allowed to run at large—such designation to terminate in 12 months unless the immune status of the dog population is maintained by revaccination. The general practice has been to give each dog only one injection of 5 ml. of vaccine, repeated yearly.

Evidence of the value of mass vaccination is adduced from the experience of 10 counties wherein 78 per cent. of the enumerated dogs were immunized; there the rabies attack rate in non-vaccinated dogs was 15·8 times as great as that in vaccinated dogs observed during the same period and in the same area.

(*b*) General recommendations for rabies control include: mass vaccination, combined with ordinary measures of dog control; anti-rabies measures to be initiated as soon as incidence is reported in adjacent counties; the appointment of a full-time veterinary consultant, on State level, to promote and supervise the control programme; the contribution of financial aid to counties for dog vaccination clinics; adequate education of the public concerning rabies.

(*c*) Control of the fox problem.—This has been attempted by the creation, through trapping, of a zone of fox scarcity surrounding the infected area.

G. Stuart

MALARIA

SNUPAREK, J. **Malaria in Czechoslovakia after World War II.** *J. Parasitology.* 1947, Dec., v. 33, No. 6, 506–8.

Although natural conditions favourable to the propagation of malaria exist in Czechoslovakia, malaria was unknown in the western parts of that country since the 1850's until the end of World War II. Then, movements of troops and civil populations, and changing epidemiological conditions caused the occurrence of malaria in two territories which are quite apart from each other, namely Southern Moravia and north-western Bohemia.

The anophelines of Czechoslovakia are found in the plains and in the lower hilly country: rarely are they found in free nature, but are mostly met with in warm quiet stables and occasionally in human dwellings. The varieties found are *A. claviger*, *A. maculipennis maculipennis* and *A. m. messeae*.

The part of Southern Moravia which was affected is flat and richly irrigated agricultural country. Wartime destruction of stables and cattle on a large scale caused the mosquitoes to lose their predominantly zoophilic character and to turn to human hosts. The retreating German armies withdrawing through Moravia were followed by the Russian army which contained Rumanian units from the highly endemic Balkans: soldiers carrying malaria parasites passed the infection on to mosquitoes and hence to the human population. Furthermore, damaged sewage and irrigation systems and bomb craters became breeding places for mosquitoes.

The affected area in north-west Bohemia was infected from a different source. This territory is a lignitic coal-mining district with many shallow shafts: in deserted and sunken mines there are undisturbed pools which breed large numbers of mosquitoes. During the war, a large synthetic petrol factory was built and labourers, including prisoners of war, were brought from many countries, such as the Balkans and Italy, to work there: among them were numerous persons with untreated malaria.

The author is unable to provide detailed statistics, as the official reports did not distinguish fresh cases of domestic origin from malaria contracted outside Czechoslovakia. He draws, however, on cases reported in the local medical journals, and refers to 14 cases in Moravia and 6 in Bohemia in the first year after the war, and 31 and 10 respectively in 1946. The increase in 1946 is explained by latency and incomplete cure and it is added that the form of malaria seen in Czechoslovakia shows a great tendency to relapse.

All infections were caused by *P. vivax* and infections with two generations, showing a quotidian fever, were common. An outstanding feature of the infection as seen in Czechoslovakia is the severe initial anaemia, characterized by red cell counts as low as 2 million per cmm. and haemoglobin often lower than 50 per cent. Such a severe anaemia is not found in the established endemic areas of Europe, and the relatively malignant course of *P. vivax* infections in Czechoslovakia is explained by lack of previous infection and a generally lowered resistance. The disease was successfully treated with the usual doses of quinine and mepacrine.

It is remarkable that no great epidemics occurred, in spite of the conditions favourable to them; it is suggested that energetic isolation and treatment helped to localize the disease.

The present importation of further labourers from the Balkans and Italy may cause a fresh wave of malaria, and this possibility must be taken into account by the health authorities for some years to come.

[This is yet another example of the disruptive effects of man-made destruction of biological equilibrium: even when such interference is benevolent—as in the case of large-scale, aerial DDT spraying and its effects on wild life, or the mutations brought about by bacterial resistance to newer chemotherapeutic agents—some of the ultimate biological implications are often unpredictable.]

H. J. O'D. Burke-Gaffney

PETA, T. L'infezione malarica a Gondar. [**Malarial Infection in Gondar.**] *Riv. di Malariologia.* 1947, Dec., v. 26, No. 6, 296–9.

The English summary appended to the paper is as follows:—

"After stating that an estimate of the malarial conditions in a certain area must be based on the human factor, surroundings and seasonal and anopheline factors, the author briefly discusses these subjects, dwelling particularly on the anopheline factor.

"From larvae breeding and the capture of culicine adults in the Gondar zone (Ethiopia), the author had following results: several specimens of *Dipterae* (*gen. Culex*) and only two *Anopheles*: *A. cinereus* and *A. demeilloni*. None of these are known to be malaria vectors. The author therefore thinks that malaria control in Gondar is unnecessary."

CIUCA, M., BALIFF, L. & CHELARESCO, M. Formes dégénérées de sporozoïtes dans l'infection expérimentale d'*A. maculipennis* v. *atroparvus* a *P. vivax* et à *P. falciparum*. [**Abnormal Forms of Sporozoites in Experimental Infection of** *A. maculipennis atroparvus* **with** *P. vivax* **and** *P. falciparum.*] *Liber Jubilaris J. Rodhain* (*Soc. Belge Méd. Trop., Brussels*). 1947, Dec., 131–46, 2 figs.

During the last 15 years work on experimental malaria has been carried out at the Socola station in Rumania. The authors used a Madagascar strain of *P. vivax* and a local strain of *P. falciparum*. Transmission to cases of G.P.I. was effected by blood inoculation and by sporozoites from *Anopheles maculipennis* var. *atroparvus*. The sporozoite infections resulted from (*a*) mosquito bites, (*b*) bites plus intravenous inoculations of glands, and (*c*) intravenous inoculations of glands alone. The second method was slightly more successful; but about 90 per cent. of all the patients developed the disease.

Fifty per cent. of 774 *Anopheles*, fed on *P. vivax* carriers, became infective: 17·7 per cent. of these infections exhibited abnormal sporozoites.

Fifty-five per cent. of 688 *Anopheles*, fed on *P. falciparum* carriers, became infective: 32·4 per cent. of these infections exhibited abnormal sporozoites.

These modifications in the appearance of the sporozoite were primarily a thickening of its body and the conversion of its chromatin into a bloated mass lying in a colourless vacuole. The shape undergoes various contortions. The abnormalities bore no apparent relation to temperature or humidity variations, nor to season.

[Examination of the protocols reveals that abnormal forms were commoner among the sporozoites which first reached the glands, and that in the older mosquitoes, degeneration was less likely to occur.] *P. C. C. Garnham*

SHORTT, H. E., GARNHAM, P. C. C., COVELL, G. & SHUTE, P. G. **The Pre-Erythrocytic Stage of Human Malaria,** *Plasmodium vivax*. *Brit. Med. J.* 1948, Mar. 20, 547.

The observations on *Plasmodium cynomolgi* by SHORTT & GARNHAM of the pre-erythrocytic stage of development in the liver of the monkey led them to suspect that *Plasmodium vivax* would be found to have a similar cycle in the liver [this *Bulletin*, 1948, v. 45, 388]. Accordingly a large number of *Anopheles maculipennis atroparvus* infected with *P. vivax* were fed on a patient at the Horton Hospital for Mental Diseases on two successive days. In addition an emulsion of infected salivary glands was injected intravenously. Seven days after the first feeding of the mosquitoes a biopsy was performed under local analgesia and a portion of liver removed for examination. In it were found plasmodial masses studded with chromatin particles very similar to those previously found in the monkey infected with *P. cynomolgi*. The masses measured up to 42μ in diameter and in some cases had the vacuoles noted in *P. cynomolgi*. There seems to be no doubt that the bodies are the pre-erythrocytic stages of development of *P. vivax* in man. The material is being studied and a further report is promised. *C. M. Wenyon*

HUFF, C. G. Periodos exoeritrociticos de los parasitos de la malaria. [**Exo-erythrocytic Stages of Malaria Parasites.**] *Medicina*. Mexico. 1948, Jan. 25, v. 28, No. 548, 25–33.

A review.

BEADLE, L. C. Note sullo sviluppo dell'*Anopheles sacharovi* sulla costa del Veneto. [**The Development of** *Anopheles sacharovi* **on the Venetian Coast.**] *Riv. di Parassit.* Rome. 1947, Dec., v. 8, No. 4, 197–203. [10 refs.] English summary (6 lines).

The highly malarious area in the north-east of Italy is limited to a coastal strip some 10 to 15 km. in width from Ravenna to Trieste. This corresponds to the area of distribution of the chief vector *A. sacharovi*. It is generally assumed that this species has a marked partiality for saline water in which to lay its eggs and that the presence of saline marshes and lagoons in this area explains the high incidence of malaria. The author's observations do not confirm this supposition. He found *A. sacharovi* breeding in water with a very low saline content. *Norman White*

THOMSON, R. C. Muirhead. **Studies on** *Anopheles gambiae* **and** *A. melas* **in and around Lagos.** *Bull. Entom. Res.* 1948, Feb., v. 38, Pt. 4, 527–58, 1 map, 3 text figs. & 5 figs. on 1 pl. [25 refs.]

The presence of an additional dark band on the palps of about one-third of female adult *Anopheles melas* in the Freetown area enables an estimate of *melas* population possible, without recourse to the laborious method of egg

distinction to distinguish *gambiae* from *melas*. This does not apply in the Lagos area, as the number of 4-banded *melas* is too small; of 1,200 egg batches examined, 99·7 per cent. were readily distinguishable into *gambiae* or *melas*.

The seasonal incidence of *melas* and *gambiae* in houses is tabulated for villages, on the coastal strip of the mainland to the north and west of Lagos Island for Lagos Town and for creek villages to the east. In the first group numbers are about equal on the coastal fringe, but *melas* fades out at a short distance (1 mile) from the coast; in Lagos town, on an island, *gambiae* is predominant; in the third group to the east, which is associated with mangrove swamp, *melas* is the most abundant. Despite these generalizations, catching stations within a short distance of each other may have widely different mosquito populations. The abundance of *melas* is mainly determined by tidal movements which are variable and unpredictable when compared to the Freetown estuary. In contrast, the abundance of *gambiae* is related to the rainfall, a great reduction in numbers occurring in the dry season, November to March. Finally, in any one village the seasonal incidence of both mosquitoes may follow entirely different courses in consecutive years.

The sporozoite rate of *gambiae* (10 per cent.) is consistently higher than that of *melas* (3·5 per cent.). Peak production of *gambiae* is associated with a lowered sporozoite rate; but in the last three months of the year when the *gambiae* population is low, the rate is higher and may reach 29 per cent. The sporozoite rate of *melas* tends to conform to the numbers of females present in houses and is comparable to the Freetown Estuary rate of 4·2 per cent. [See TREDRE, this *Bulletin*, 1947, v. 44, 488.] Observations on resting places, both indoor and outdoor, indicate that *gambiae* in the gravid state made use of the house to a much greater extent than did gravid *melas*; in one village it was estimated that through the favourable six months of the year, *melas* made use of outside resting places to 10 times the extent that *gambiae* did. The degree to which *gambiae* or *melas* favour outside resting places is of considerable importance in relation to the use of residual insecticide in houses as a control measure.

The movement of mosquitoes in and out of houses was investigated by the use of experimental huts fitted with a special window trap; this method resulted from the observation that exterior waning light is a powerful attraction to mosquitoes indoors. It was noted that 90 per cent. of blood feeding by *melas* and *gambiae* took place after midnight, the period of greatest activity being between 4 a.m. and dawn; 43 per cent. of *melas* and 26 per cent. of *gambiae* which had entered and fed left by dawn the same night. In the case of *melas* which remained in the hut, all gravid and 70 per cent. of half-gravid females left at dusk.

The author was successful in getting swarming, mating and fertilization of *melas* and *gambiae* to take place in 1 ft.-cube cages. Data of cross-fertilization experiments are quoted; hybrid males were sterile.

The breeding areas of *melas* are very difficult to localize and the whole tidal swamp area covered with *Paspalum* is suspect; the comprehensive nature of the tidal swamp reclamation should eliminate all potential breeding places [GILROY and CHWATT, this *Bulletin*, 1945, v. 42, 786]. Breeding areas of *A. gambiae* are the typical open shallow water collections, which include almost dry wells, rain pools and puddles and sedge swamps. The last-named may be just below high water mark and prolific breeding will cease abruptly if a fortuitous tide floods the area. In Lagos Town, the steady progress in street drainage and swamp filling has practically eliminated breeding places. However, the author draws attention to the instance of a single small garden-compound producing in the rainy season a *gambiae* output sufficiently enormous to affect a whole corner of the city and nullify good work in process elsewhere.

[There is no reference to the possibility of the invasion of Lagos Town by *melas* from across the surrounding waters and the evidence of this paper suggests that, after the extensive swamp reclamation measures in the district, the town and port may be kept relatively free of malaria vectors by a vigilant sanitary staff.] *R. Ford Tredre*

SCHWETZ, J. Sur le lac Tumba. Notes géographiques, entomologiques et médicales. (Moustiques et paludisme ; tsétsés et trypanosomiase.) [**Lake Tumba. Geographical, Entomological and Medical Notes : Mosquitoes and Malaria ; Tsetse Flies and Trypanosomiasis.**] *Inst. Roy. Colonial Belge. Bull. des Séances.* 1947, v. 18, No. 2, 482–511, 1 map & 3 figs. on 2 pls.

Lake Tumba lies near the left bank of the River Congo, about 100 kilometres south of the Equator. A winding channel about 15 km. long unites the waters of lake and river. Such little current as is manifest in this channel is towards the lake in the rainy season and towards the river when the water is low. The lake is about 45 km. long (north–south) and about 22 km. broad ; its shores are indented by very numerous bays and capes. Several rivers discharge into the lake, the two largest being the Lola, into the south of the lake, and the Ngombe, into the north-east.

The author spent three weeks investigating conditions on the shores of Lake Tumba, making his headquarters at Bikoro, about the middle of the eastern shore. A motoring road, 128 km., joins Bikoro to Coquilhatville which lies on the Equator almost due north of the lake.

The banks of the lake are for the most part high and gently sloping, wooded and without grassy or marshy edge favourable to mosquito breeding ; in such places mosquitoes are almost non-existent. But on certain small bays, near villages, swampy conditions near the mouths of small streams are productive of mosquitoes ; these are still more numerous near the mouths and along the banks of the larger rivers.

A. obscurus and *A. paludis* were the most prevalent *Anopheles* along the shores of Lake Tumba ; these two species are in general rather rare in this part of the Congo and neither has been incriminated as a vector of malaria. *A. marshalli* var. *moucheti*, the predominant anopheline at Coquilhatville, was rare, as was *A. gambiae*. *Aëdes aegypti* was not found. *Mansonioides* were very rare.

Glossina palpalis was rare along the shores of the lake, but very prevalent along the banks of the rivers that flow into it. Several specimens of *G. tabaniformis* were also captured.

Similium albivirgulatum was very prevalent along the shores of the lake : they bit during daytime but were most active towards evening. Phlebotomi were also plentiful, *Ph. africanus*, *Ph. africanus* var. *niger*, *Ph. decipiens* and *Ph. schwetzi*.

The blood of 448 inhabitants of four lakeside villages was examined. This showed malaria to be endemic ; parasite rates were high but the number of parasites was low. *P. falciparum* was by far the most prevalent species. *P. vivax* was only found in two films. *Acanthocheilonema perstans* was frequently encountered ; *Loa loa* occasionally.

The author found a considerable number of villagers who were undergoing treatment for sleeping sickness or who had been treated, but little or no evidence that they were or had been infected. The diagnoses had been made on altogether insufficient evidence. In only one of the 448 individuals examined, thick drop and smears, were trypanosomes discovered ; he was a schoolboy in the Catholic Mission School at Bikoro. Sleeping sickness exists in this region but cases are extremely rare. *Norman White*

MILLER, A., BURGESS, R. W. & CARPENTER, S. J. **Potentialities of Transportation of Exotic Anophelines by Airplane.** *J. National Malaria Soc.* 1947, Dec., v. 6, No. 4, 227–43. [27 refs.]

The number of aeroplanes entering the United States of America each year is estimated to be 35,000, or nearly 100 per day. This volume of air traffic is increasing and the time spent on journeys is being reduced, so that very soon no place will be more than two days' flight from the U.S.A. The bulk of the traffic at present comes from Latin America and it might be expected that the greatest danger of importing mosquitoes lies in that quarter, but from the climatic point of view, Europe and the non-tropical areas correspond more closely with conditions in the U.S.A. as a whole, and it may be more likely that species transported from such places would be more easily established.

The authors review the history of the development of international air traffic and discuss the practical application of the "International Sanitary Convention for Aerial Navigation." Figures are quoted from reports showing, for example, that in the year July 1st, 1944 to June 30th, 1945, 1,418 mosquitoes (158 alive) were among 24,930 insects found on 12,367 aircraft. There were 1,339 culicines (142 alive) of 21 species and 79 anophelines (16 alive) of 9 species. The identified anophelines were *Anopheles albimanus*, 10 alive out of 34 found, *A. pseudopunctipennis*, 2 alive out of 4, *A. quadrimaculatus*, 3 alive out of 5, *A. punctipennis*, 1 living, *A. crucians*, 19 dead, and 1 dead specimen of each of the following, *A. grabhami*, *A. maculipennis aztecus* (?), *A. neomaculipalpus*, and *A. pharoensis*. The last-named and one Indian culicine are the only Old World species in the reports that are not already present in the U.S.A.

It is thought that not more than 10 per cent. of mosquitoes are detected in the planes, and the authors speculate on the hypothetical number of exotic mosquitoes likely to be imported in one year and arrive at the following figures for 100 aircraft: 115 mosquitoes (13 alive), 6·4 anophelines (1·3 alive), and 1 exotic species including 0·3 to 0·6 exotic anophelines. At this calculation 35,000 aircraft would bring in 350 exotic mosquitoes of which 100 to 200 might be anophelines not already recorded in the States or 10 to 25 living anophelines per year; but during the last three years, no viable anopheline has been detected in the incoming aircraft, owing to the efficiency of the preventive measures. Nevertheless, in spite of the small chances of importation of these mosquitoes, prudence and experience demand a continuance and extension of mosquito control around airports, and the disinsectization of the aircraft. The efficiency of insecticides is improving, as also are the methods of application; and the likelihood of new malaria vectors becoming established in the United States remains, in the opinion of the authors, a potential problem but not an acute one. *H. S. Leeson*

GIGLIOLI, G. **An Investigation of the House-frequenting Habits of Mosquitoes of the British Guiana Coastland in relation to the Use of DDT.** *Amer. J. Trop. Med.* 1948, Jan., v. 28, No. 1, 43–70, 6 figs. & 1 graph.

In the first quarter of 1945, SYMES and HADAWAY [this *Bulletin*, 1945, v. 42, 785] initiated in British Guiana the spraying of houses with DDT. Progressive expansion of this work necessitated preliminary mosquito surveys of which this paper is descriptive. These were confined to the coastal zone, the topography and meteorology being briefly referred to. The precise localities selected for description can be taken as prototypes of ecological conditions prevailing in urban, suburban, village and rural areas of the coastland of British Guiana. [Several excellent photographs are included.] Monthly morning mosquito captures in houses are tabulated for each locality for periods varying from two

to fifteen months. In one locality, an experimental hut enabled 2-hourly night catches to be recorded; a Shannon dawn trap with animal bait was used in this area primarily to estimate the *A. aquasalis* population, but a table of all captures is given.

The mosquito species encountered were nine in number, of which *A. aquasalis*, *A. albitarsis* and *Uranotaenia* (species not determined) were rare. *Aëdes taeniorhynchus* and *Aëdeomyia squamipennis* rarely frequent houses; *Aëdes aegypti* is subject to control measures. *Culex fatigans* and *Anopheles darlingi* accounted for 66 and 26 per cent. respectively of all captures. *Mansonia* varied in different localities. A description is given of the habits, breeding places, etc., of each of the above mosquitoes.

The average *A. darlingi* (the malaria vector) catch per room is as follows :—

Locality	Surroundings	Mosquito Catch per room
Lusignan (East coast)	Irrigated cane lands	34·7
Triumph village (East coast) ...	Irrigated cane lands, inland rice fields and provision gardens	46·1
Mon Repos pasture (East coast)	Open ventilated front land pastures and rice fields	0·96
Lodge village	Georgetown suburb	1·05
Wortmanville	Georgetown city ward	0·33
La Grange (West bank, Demerara)	Irrigated inland rice fields and provision gardens	22·2

The author concludes that the highly domestic biting and resting habits of *A. darlingi* and *Aëdes aegypti* render the prospects of control by DDT house-spraying [as a residual insecticide] excellent.

Culex fatigans is variable in its biting and resting habits and it is expected that this control method will have little effect on the total incidence.

R. Ford Tredre

LUCREZI, G. Citomorfologia e dinamica midollare nelle prime fasi della malaria indotta. [**The Bone Marrow in the Early Stages of Induced Malaria.**] *Riv. di Malariologia.* 1947, Dec., v. 26, No. 6, 267–82.

The English summary appended to the paper is as follows :—

"The author studied the behaviour of the haemopoietic marrow in 6 progressive paralytic patients inoculated with *Anophelines* (5 *Pl. vivax* and 1 *Pl. falciparum*). The sternal punctures were carried out in series, beginning before the inoculation and continuing until the outset of the disease.

"The author, having thus established the starting ground (anatomical functioning of the marrow in the progressive paralytic patients), studied the results following inoculation and observed that during the incubation period and the very first phases of the disease the marrow assumes a prevalently erythroblastic orientation, without a constant and prevailing reaction of the reticulum-endothelium."

KLEEBERG, J. & BIRNBAUM, D. **Studies on Liver Damage in Acute Malaria.** *Trans. Roy. Soc. Trop. Med. & Hyg.* 1948, Jan., v. 41, No. 4, 555–66, 4 graphs. [23 refs.]

The authors have investigated the Weltmann reaction in 96 cases of naturally acquired *P. vivax* and *P. falciparum* malaria. This reaction measures the

coagulability of the patient's serum in solutions of calcium chloride; this is apparently governed in some way by the globulin content. Sixty-six cases showed increased coagulability. Of these, a high percentage showed changes in cephalin-cholesterol and cholesterol ester fractions of the serum, but there was no correlation between the degree of this reduction and value of the Weltmann reaction, red cell count or sensitivity of the erythrocytes to lysis in bile solution [MER *et al.*, this *Bulletin*, 1941, v. 38, 562]. On the other hand, there was a close relation between changes in the Weltmann reaction (a shift to the right: *i.e.*, coagulation of serum in lower calcium chloride concentrations than normal) and the sensitivity of the erythrocytes to lysis in bile solution.

According to the authors, the results of the Weltmann reaction and the Chorine test (both of which are dependent on certain serum globulins) indicate hepatic damage, since the globulins are synthesized in the liver. Kleeberg claims that "since in all acute haemolytic anaemias the W.R. (*sic*) quickly shifts markedly to the right, a sudden shift" (to the right in the Weltmann reaction) "in malaria is probably indicative of imminent blackwater fever."

[It would be more profitable at this stage to investigate quantitatively the changes in plasma proteins which actually occur in malaria (as for example, was attempted by DOLE and EMERSON, this *Bulletin*, 1946, v. 43, 624) than to multiply tests which appear basically non-specific.

The authors' habit of referring to the Weltmann reaction as the "W.R." is both irritating and confusing.] *B. G. Maegraith*

RADVAN, I. & APREOTESCI, C. La bilirubinémie paludéenne par rapport à la physiopathologie et à la thérapeutique. [**Malarial Bilirubinaemia in relation to Pathology and Treatment.**] *Riv. di Malariologia.* 1947, Aug., v. 26, No. 4, 183–90.

BYLMER, J. & WINCKEL, C. W. F. **Induced Malaria for Treatment of General Paralysis.** *J. Trop. Med. & Hyg.* 1948, Feb., v. 51, No. 2, 27–33, 2 charts.

A centre for the provision of malaria parasites for the treatment of general paralysis of the insane in Holland was started in 1921. This article, by two malariologists who have studied malaria in the field and at the Psychiatric Clinic in Amsterdam, deals with some of the many problems encountered in connexion with induced malaria as employed for therapy purposes. The two species of malaria parasite used are *P. vivax* and *P. malariae*. *P. vivax* is preferable to *P. malariae* because it produces the necessary number of chills and is readily controlled by anti-malarial drugs.

It is pointed out that infection is readily produced by infected blood and by infected mosquitoes. One advantage of inducing fever by blood inoculation is that the patients never relapse; but, on the other hand, there is some risk of bacterial contamination by this method, especially when some time elapses between taking parasitic blood from a donor and injecting it into the recipient.

For some time the local indigenous strain was used, but this was not very satisfactory: it was found that with the local strain the incubation period was frequently of long duration, six to nine months. The Horton (Madagascar) strain is now used and is proving more satisfactory. Patients who are found to be immune to *P. vivax* are infected with *P. malariae* and fever develops satisfactorily as there is no cross immunity between the species. *P. falciparum* is not used, as it is considered to be too dangerous. The authors state that the number of patients admitted to their clinic is too few to warrant the employment of three different strains of parasite. [Presumably they mean *species* and not *strains*.]

Although *P. malariae* has been employed at their clinic for many years, on only one occasion have they succeeded in infecting the local vector (*Anopheles maculipennis* var. *atroparvus*), in 1935.

Failure to infect patients by direct blood inoculation seldom occurs when patients are inoculated at the Clinic, although many failures take place when citrated blood is sent through the post. It is believed that the reason for failures is that most of the parasites die in transit. The incubation period is longer, presumably because most of the parasites have died.

Whenever possible, the paretics are allowed to have 10 or 12 attacks of fever with temperatures of 104°F. In such cases relapses are few, even when infection is induced by mosquito bites. This, it is believed, is because by the end of the fever period most of the patients have become immune. Often the fever is quotidian (*P. vivax*), but this is easily changed to tertian by giving a single intravenous dose of neoarsphenamine (75 mgm.) which has a selective destructive action on the half-grown trophozoite.

In the case of the Horton Madagascar strain, compared with the endemic Dutch strain, only half of the dose of this drug is needed to change the fever from quotidian to tertian. It was found that there is a mutual homologous immunity between the Madagascar and the Dutch strains. Even patients who have had natural benign tertian infections in Holland are immune to the Madagascar strain. Primary cases of *P. vivax* malaria usually show two or three days of "initial fever". Patients who do not show this initial fever tend to go on to a spontaneous recovery before the desired number of attacks has occurred, owing, the authors believe, to the patients' immunity.

The article concludes with advice to those who employ malaria therapy on the preservation of parasite strains and how to treat the fever after the desired number of attacks has been attained; reasons are also given why blood films of patients undergoing malaria therapy should be examined frequently during the fever period. *P. G. Shute*

PUTNAM, P., BOYD, M. F. & MEAD, Pauline A. **Periodic or Cyclically Recurring Phenomena of Vivax Malaria Infections.** *Amer. J. Hyg.* 1947, Sept., v. 46, No. 2, 212–47, 14 figs. [12 refs.]

A statistical analysis was made of data concerning the parasitaemia of 70 white patients with naturally induced *P. vivax* infections (McCoy strain). Each patient experienced a primary attack of at least 3 weeks and a period of patency lasting until the 72nd day after inoculation. Forty patients had recrudescences; 30 had none. The records of each of these two groups were again divided according as to whether the prepatent period ended on an odd or even day. Logarithmic mean parasite counts were computed for each day of the period of observation for each of the four groups, with the data referred first to the day of inoculation and second to the day of first appearance of parasites.

Parasites first appear on an average 12 days after inoculation; the parasite density rises steeply to a peak 12 days later and then declines gradually. A significant 12-day cycle was observed in three of the four groups. A 16-day cycle characterized the parasitaemia of 26 patients without recrudescences and with even-day prepatent periods, but when the observed crests of the recurring cycles were synchronized it was found that the parasitaemia of 11 followed a 12-day rhythm, that of 9 followed a 16-day cyclical course, while that of the remaining six showed no cyclical trend. A significant 16-day cycle was revealed in the parasitaemia of 4 patients extending over 90 days after inoculation.

Either the day of inoculation or of the first appearance of parasites may become the point of reference once the primary division of patients is made on

the basis of prepatent periods. The first paroxysm is not a desirable point of reference.

Evidence of brood dominance was afforded by the parasitaemia of 15 patients with even-day prepatent periods and no recrudescences; the mean counts were significantly higher on odd days following inoculation. Six of these patients had primary attacks predominantly tertian in character with paroxysms on even days.

A statistical study was also made of data concerning recrudescences, and their prior remissions of two days or more, of the 40 patients. The purpose of the study was to determine whether the days of onset of recrudescences and remissions follow a rhythmical pattern; whether such pattern is related to the cyclical trend of parasitaemia previously determined, and whether their timing shows dominance in the activity of one brood of parasites over that of the other. The data were referred to the day of inoculation, the day of first appearance of parasites, and the day of the first paroxysm of the primary attack.

A significant 12-day rhythm was indicated by the days of onset of recrudescences. In patients with odd-day prepatent periods the clustering of events was most clearly defined when the onsets were referred to the day of first parasites. For patients with even-day prepatent periods the rhythm was most evident when the data were referred to the day of first paroxysm. A significant 12-day clustering of remissions was evident only for patients with odd-day prepatent periods.

Remissions increase in length as recrudescences grow shorter though no significant correlation between their durations was determined. Recrudescences averaged 6·2 and 7·2 days in length for the two groups of patients while remissions averaged 5·8 days for each. Thus the length of the two intervals combined was 12 and 13 days respectively.

Paroxysms initiating the primary attack and those immediately preceding and following remissions are as likely to occur on odd as on even days; this affords no evidence of the dominance of one or other brood of parasite.

The authors offer no explanation of the cyclical phenomena observed. These may be due to some unknown aspects of the schizogonous cycle of the parasites or to intermittent activity of the host's defence mechanism. *Norman White*

KULCSAR, D. D. **Effect of Malaria on Pregnancy.** *Canadian Med. Ass. J.* 1947, Oct., v. 57, No. 4, 332–7. [17 refs.]

A study of the effects of malaria on the course of pregnancy, based on admissions from May 1st, 1946 to the end of April 1947 to the Obstetrical Department of the Kweilin Provincial Hospital, the admissions totalling 360 cases. The Province of Kwangsi, with its capital Kweilin, is stated to be one of the worst malarial districts in China. No accurate data are available, but it is estimated that at least 50 per cent. of the population suffer from malaria.

In the series under review, 59 cases (17 per cent.) showed a positive blood smear on examination, while 173 gave a definite past history of malaria (48 per cent. of admissions). Eight patients were treated on clinical signs alone. Of 59 patients definitely proved to be positive on blood examination, 19 had premature labour (period of gestation not given) and 9 had threatened or incomplete abortion, *i.e.* 48 per cent. of abnormal cases compared with 18 per cent. of abnormalities in the so-called malaria-free group (120) cases.

The type of infection in the 59 positive cases was: *P. vivax*, 26 (44·3 per cent.); *P. falciparum*, 33 (55·7 per cent.); *P. malariae*, nil; one case of mixed *vivax* and *falciparum* infection. From a study of the literature and from

following up some of his cases, the author believes in the occurrence of congenital malaria.

The author thinks that a past history of malaria has no adverse effect on the course of pregnancy, except as regards the possibility of recurrence, *P. vivax* infections being rather more liable to relapse than *P. falciparum* (55 as compared to 45 per cent.). Of the 59 blood positive cases, 50 were recurrences and only 9 were primary infections. It is thought that most of the recurrences would have been prevented, most of the premature labours continued to term and some of the stillborn infants born alive had suppressive anti-malarial medication been consistently used.

While the author agrees that the most thorough search should be made for any possible cause of fever, he suggests that there should be no delay in administration of mepacrine or quinine where there is any clinical suspicion of malaria. Leucopenia and relative mononucleosis are regarded as valuable signs of a malarial infection.

The Kahn test was positive in 11 per cent. of cases with positive blood smears or a past history of malaria, as against 7 per cent. in malaria negative cases.

MANSON-BAHR (*Manson's Tropical Diseases*, 12th ed. 1945) considers that malaria *per se* is a far more potent oxytocic than any drug. However he recommends care in giving quinine as if it is administered in large doses it may sometimes cause miscarriage ; but ACTON, as cited in the same work, thinks that miscarriage can only be caused by doses of quinine large enough to poison the patient. [The reviewer, in the course of a fairly wide experience, has come to the same conclusion, in fact he has found that the most efficient abortifacient is a smart attack of subtertian malaria left untreated for a few days.]

Mepacrine was found to be well tolerated by pregnant women in relatively large doses and is replacing quinine in pregnancy, although opinions still differ as to its efficacy as compared with the latter drug. With the usual plan of dosage, an effective plasma level was found to be attained more rapidly with quinine than mepacrine.

The author treated 30 cases with quinine and 20 with mepacrine. Fifty per cent. of cases treated with mepacrine were controlled after one febrile attack, but only 22 per cent. of those treated with quinine were so controlled. No untoward effects were experienced with either drug, but it is considered that paludrine will probably be the drug of choice in the near future. Contrary to previous reports, the author does not think that malaria is a serious predisposing cause of toxaemias. *C. F. Shelton*

BILIANGADY, N. W. **Spontaneous Rupture of the Spleen following an Attack of Malaria : its Causes.** *Indian Med. Gaz.* 1947, Sept., v. 82, No. 9, 539–41.

CHEN, G. & GEILING, E. M. K. **The Acute Joint Toxicity of Atabrine, Quinine, Hydroxyethylapocupreine, Pamaquine and Pentaquine.** *J. Pharm. & Exper. Therap.* 1947, Oct., v. 91, No. 2, 133–9, 5 figs.

Combinations of quinine and plasmoquine (pamaquin) were used in the treatment of *P. vivax* malaria by SINTON & BIRD [this *Bulletin*, 1929, v. 26, 14] soon after the discovery of the latter drug. Atebrin (mepacrine) and plasmoquine were similarly used by MÜHLENS & FISCHER [this *Bulletin*, 1932, v. 29, 706] in the treatment of malignant tertian malaria. The present authors have investigated the acute joint lethal toxicities for mice of certain pairs of the drugs named in the title. Mice of 18 to 26 gm. weight were used in groups of 20 for each test and were injected intraperitoneally with a definite volume of solution based on body weight. It did not materially affect the results whether the two drugs were given in one solution or separately. Deaths were recorded after

an observation period of two days. Quinine and atebrin acted independently and similarly as regards toxicity; so also did quinine and hydroxyethyl-apocupreine. In the case of atebrin and pamaquin, the lethal effect of the latter was not influenced by a sublethal dose of the former, indicating that the two substances act independently but in different ways. The mortality when atebrin was used in the lethal range was, however, greater than expected. Quinine with plasmoquine and also quinine with pentaquine (chemically related to pamaquin) displayed a synergistic action as regards toxicity. A similar synergistic action of these substances was displayed in their therapeutic action on avian malaria. The explanation suggested is that quinine and pamaquin may act on different stages in a vital enzymatic process. *J. D. Fulton*

ELDERFIELD, R. C., KREYSA, F. J., DUNN, J. H. & HUMPHREYS, D. D. **A Study of the Synthesis of Plasmochin by the Reductive Amination Method with Raney Nickel.** *J. Amer. Chem. Soc.* 1948, Jan., v. 70, No. 1, 40–44, 2 figs.

BROWN, B. R. & HAMMICK, D. L. **A Resolution of Mepacrine [2-Chloro-5-(δ-Diethylamino-α-Methyl-Butyl) Amino-7-Methoxyacridine].** *J. Chem. Soc.* 1948, Jan., 99–100.

ANDREWS, W. H. H., GALL, D. & MAEGRAITH, B. G. **Studies on Synthetic Antimalarial Drugs. XIX. The Effect of Therapeutic Courses of Paludrine on the Relapse-Rate of Vivax Malaria.** *Ann. Trop. Med. & Parasit.* 1947, Dec., v. 41, Nos. 3/4, 375–9, 1 fig.

The relapse rate in *P. vivax* infections after administration of a therapeutic course of atebrin (mepacrine) consisting of 200 mgm. thrice daily for 2 days followed by 100 mgm. thrice daily for 10 days to patients having clinical attacks, was compared with that of two similar groups of patients treated with paludrine. The dosages of the latter were 500 mgm. twice daily for 14 days and 50 mgm. twice daily for 14 days respectively. The cases were not specially selected, infection having been acquired by most patients in the Far East and by a few in the Mediterranean. A follow-up of 92 cases was made for 6 months, by means of postcards. For assessment of results, only those relapses were considered which occurred within this period after treatment. The results with paludrine were similar to those obtained by JOHNSTONE [this *Bulletin*, 1947, v. 44, 284], and the relapse rate was approximately the same on the three different dosage schedules. In a separate experiment, patients were given an initial dose of 10 to 300 mgm. paludrine and thereafter 100 mgm. weekly for six months. The follow-up after treatment was again made by post, cards and microscope slides being provided; the latter were to be returned with a thick blood film if relapse was suspected. By this means, the follow-up period for 79 patients was not less than 1 year in each case. The total number of relapses was 15, and the relapse rate was lower than those rates which followed the dosage schedules described above. *J. D. Fulton*

CHEN, K. K. & ANDERSON, R. C. **The Toxicity and General Pharmacology of N_1-*p*-Chlorophenyl-N_5-Isopropyl Biguanide.** *J. Pharm. & Exper. Therap.* 1947, Oct., v. 91, No. 2, 157–60. [10 refs.]

The authors have made observations on the pharmacology and toxicity of paludrine in various laboratory animals with results which are summarized as follows.

" 1. The acute toxicity of N_1-*p*-chlorophenyl-N_5-isopropyl biguanide HCl has been compared with quinine 2HCl and quinacrine HCl in mice, rats, guineapigs, and rabbits.

"2. The biguanide has been repeatedly administered in various doses to rats. No pathologic lesions can be demonstrated, and death from large doses may be attributed to acute systemic effects.

"3. The biguanide lowers blood pressure with an acceleration of respiratory rate in anesthetized cats.

"4. With the exception of the isolated guineapig's uterus, which responds by contraction, the biguanide has an inherently relaxing property on the isolated rabbit's uterus and intestine, and the isolated guineapig's intestine.

"5. The action of the biguanide on the blood sugar of rabbits is suggestive of a slight hypoglycemia." *J. D. Fulton*

DESHMUKH, P. L. **Treatment of Relapsing Malaria with Specific Antimalarial Drugs in combination with Penicillin.** *Indian Med. Gaz.* 1947, Sept., v. 82, No. 9, 511–14. [13 refs.]

McCOUBREY, A. & WEBSTER, W. **Contributions to the Chemistry of Synthetic Antimalarials. Part V. Attempted Synthesis of 6-Methoxy-8-Quinolyl-α-Dialkylaminomethylcarbinols.** *J. Chem. Soc.* 1948, Jan., 97–9.

WYNNE-GRIFFITH, G. **Suppression of Malaria by Mepacrine.** *J. Roy. Army Med. Corps.* 1947, Sept., v. 89, No. 3, 112–21, 5 figs.

This paper relates experiences in Burma during the recent war. The striking fall in malaria morbidity rates that followed the prophylactic administration of mepacrine in 1945 is described. Similar success was achieved among Japanese prisoners of war. *Norman White*

VINE, J. M. **Malaria Control with D.D.T. on a National Scale—Greece, 1946.** [Abridged.] *Proc. Roy. Soc. Med.* 1947, Nov., v. 40, No. 13, 841–8 (Sect. Epidem. & State Med. 43–50).

This is a description of a nation-wide attempt that was initiated by UNRRA to eradicate malaria from Greece. DDT was the sole weapon employed. A trial of the ground methods was made in 1945. The resulting fall in malaria incidence and the eradication of insect pests were so satisfactory that the Greek Government allocated £300,000 for the major onslaught in 1946. The organization was based on UNRRA Headquarters at Athens and the Malaria Division of the Athens School of Hygiene. In each of 11 divisions into which the country had been divided, there was a Greek malariologist, an American sanitary engineer of the U.S. Public Health Service, Greek sanitary engineers, and Greek inspectors and foremen trained in the technique of preparing DDT mixtures and of spraying. These specialists hired gangs of labourers and trained them to do the actual work. For the eradication of hibernating mosquitoes 5 per cent. DDT in either kerosene or Diesel oil was used at 220 mgm. per square foot. In April, larvicidal work was commenced. Water accumulations up to 5 kilometres from village or hamlet were sprayed with 5 per cent. DDT in Diesel oil. This continued throughout the summer until September 30. Up to November 1, about 700,000 houses and outbuildings were sprayed.

Aeroplanes were used for spraying marsh lands. Eighteen small training planes of the U.S.A.A.F. Stearman type were employed. The area to be sprayed, determined by larva surveys, was 113,000 acres at the beginning of the season: this shrank to 80,000 acres during the dry summer. It was sprayed 5 times. DDT, 20 per cent. in Velsicol, was used for all aeroplane work. Under ordinary conditions a pilot could spray about 17 acres per minute.

The side-effects of DDT spraying were interesting. In Athens in 1946 there was an almost total absence of flies. In addition to the spraying of houses, large garbage dumps near the city were sprayed from the air at intervals during the

summer. Sandflies disappeared from the Nea Smyrna suburb of Athens. Air-spraying was effective against the Dacus fly in olive groves and against a plague of Tene moth in pine and fruit trees. A fall in the notifications of dysentery from July onwards may have resulted from a destruction of flies.

The incidence of malaria was much below the expected level; comprehensive statistical data are not available. It is estimated that some 3,600,000 persons were protected, about 80 per cent. of the population at risk. The overall cost per head was two shillings.

An addendum to the paper enunciates the following conclusions and principles :—

(1) Comprehensive data on all aspects of the areas to be dealt with are essentially required in advance.

(2) Complete co-operation is required between all sections engaged in the operation; this includes Government, technical and administrative staff and the public; the public must be kept fully informed of developments.

(3) The time-factor of anopheline habits must be taken into account: *e.g.*, in Greece *A. elutus* and *A. maculipennis* must be attacked in April, while *A. superpictus* may be overlooked until June–July.

(4) Where possible, blood, spleens and "baby rates" should be studied over typical bad malaria areas before and just after the season.

(5) It is an advantage to make a final onslaught on breeding sites at the end of the season, in order to diminish hibernators.

(6) It was found that there was little or no mortality among bees where DDT was used after blossom time: this compares favourably with mortality from other forms of chemical insect controls on fruit and vegetables. On the other hand, when DDT was used in a house where silkworms were breeding, these were inevitably killed.

(7) From experience of 6,000 labourers over six months, it is stated that the toxic effect of DDT on human beings is negligible: the effect on the skin of kerosene and oil must, however, be taken into account.

(8) There are a number of questions still to be answered regarding the activity of DDT, such as the optimum contact time per area, the relative value of larvicidal methods and house-spraying, the best agents for preparing emulsions, the optimum *para-para* content of technical grades of DDT, the effects of temperature and storage, and the most suitable containers for DDT: much experimental work is still required towards determining the most satisfactory and economic use of DDT in large-scale malaria control schemes.

Norman White

AFRIDI, M. K. & BHATIA, M. L. **Malaria Control of Villages around Quetta (Baluchistan) with D.D.T.** *Indian J. Malariology.* 1947, June, v. 1, No. 2, 279–87, 1 folding map.

In rural villages in the Quetta district (30°N. 67°E.), the incidence of malaria is high in the transmission season from mid-July to mid-September. A pilot control scheme in a limited number of villages (20,000 population) was instituted in 1946 with the following aims and objects to find :—

(*a*) Whether malaria in a rural population in Baluchistan could be controlled simply by killing adult mosquitoes by periodic DDT spraying;

(*b*) Whether the cost *per caput* on such control measures would be within reasonable economic bounds; and

(*c*) Whether spraying operations could be conducted in a community in which the purdah system (seclusion of women) rendered entry into houses difficult.

The villages concerned are described. A 25 per cent. DDT emulsion concentrate diluted with 9 parts of water gave a spraying solution containing

2·5 per cent. DDT. The dosage applied to wall surfaces was estimated to be 1 to 1·5 cc. per sq. ft. (25–38 mgm. DDT per sq. ft.). Three distinct groups of villages were treated once by outdoor spraying [the surfaces treated are not defined] between July 22nd and August 2nd ; four weeks after this first spraying, one group was re-treated indoors, one group outdoors and one group by a combination of indoor and outdoor spraying. The vector mosquitoes were *A. superpictus*, *A. culicifacies* and *A. stephensi*.

A table summarizes the quantities of DDT used and man-hours expended. The cost of two sprayings amounted to 2·4 annas *per caput*, but a single indoor application of DDT emulsion would be effective for one malaria season at a cost of 1·4 annas exclusive of medical supervision.

The results, as assessed by spleen and parasite rates in children in June and September, showed a definite effect in lessening the intensity of malaria transmission in two groups of villages, whereas in the third group which had been treated by both indoor and outdoor spraying no decrease occurred ; this was believed to be due to malaria infections contracted in neighbouring untreated villages. The decrease in spleen rates in the favourable groups were 31 to 28 and 45 to 35 per cent. respectively, whereas untreated control villages showed that the usual degree of malaria transmission caused a rise in spleen rate of 36 to 66 per cent. between June and September. No insuperable difficulties were encountered in gaining entry into the house for spraying, despite the local purdah system. *R. Ford Tredre*

HAWKING, F. & HUNT, R. **The *kochi* Type of Malaria Parasite in Monkeys.** *Liber Jubilaris J. Rodhain* (*Soc. Belge Méd. Trop., Brussels*). 1947, Dec., 251–66, 13 coloured figs. on 2 pls. & 5 figs. [20 refs.]

In the blood of a baboon received from the Gambia a malarial parasite identified as *Plasmodium kochi* was found. The parasite occurred as mature gametocytes and ring forms of various sizes. It transpired that the ring forms were immature gametocytes and nothing in the shape of asexual development occurred in the blood. Fresh batches of rings appeared in the blood from time to time. The spherical gametocytes shown on a coloured plate, when mature, appear to be extracellular. Batches of *Anopheles quadrimaculatus*, *Anopheles maculipennis atroparvus*, *Aëdes aegypti* and *Culex molestus* were fed on the baboon. Of 771 mosquitoes, a few oöcysts were seen in the stomachs of 3 *Anopheles quadrimaculatus* and one *Anopheles maculipennis atroparvus*. With the appearance of GARNHAM's description [this *Bulletin*, 1947, v. 44, 882] of the large schizonts of *P. kochi*, the authors examined the liver of the infected baboon and found a number of yellow nodules in the liver. These were sectioned and appeared to be degenerated schizonts. Owing to the absence of schizonts from the blood, the authors conclude that the parasite is not a *Plasmodium* but a *Haemoproteus*. The paper is illustrated by 2 coloured plates and 2 black and white plates. Stages of schizogony figured are from Garnham's sections and smears. *C. M. Wenyon*

CRUZ, W. O. & DE MELLO, R. P. Infecção do macaco sul americano " saguí " (*Callitrix jacchus*, Linneus 1758) com o *Plasmodium knowlesi*. [**Infection of the South American Monkey,** *Callitrix jacchus*, **with** *Plasmodium knowlesi*.] *Mem. Inst. Oswaldo Cruz.* 1947, Mar., v. 45, No. 1, 119–21.

The English summary appended to the paper is as follows :—

" Infection of the South American monkey " Saguí " (*Callitrix jacchus*, Linneus 1758) after inoculation with *Plasmodium knowlesi* have been observed. Intravenous massive inoculation brings death in about ten days. With intramuscular inoculation of smaller quantities of parasites, spontaneous cures have

been verified several times. The known 24 hours cycle as well as the morphological characteristics of the *Plasmodium knowlesi* as observed in Rhesus infections, remain the same in the monkey studied.

" The vigor of *Callitrix jacchus* when kept in captivity is definitely less than that observed with Rhesus monkeys, but as its buying cost is thirty times less, it could be considered a useful new experimental animal for malaria research."

MULLIGAN, H. W. & SOMMERVILLE, T. **Malaria in the Malabar Squirrel.** *Indian J. Malariology.* 1947, June, v. 1, No. 2, 329–35, 30 coloured figs. on 1 pl. [10 refs.]

The authors place on record observations made on a blood parasite of the Malabar squirrel (*Sciurus indicus malabaricus*). The work was interrupted by the 2nd World War and was never completed. [These authors, however, appear to have made further studies on the same parasite, in the course of the Mammalian Malaria Enquiry—see this *Bulletin*, 1947, v. 44, 966. They were again unsuccessful in finding exo-erythrocytic stages. In the latter paper the parasite is referred to as *P. ratufae*.]

The squirrels are found in the dense forests of the Nilgiris, and they live in the upper strata of the trees. Seven out of nine adult animals exhibited the parasites in the blood, chiefly as mature gametocytes. The trophozoites are stated to be scanty and not to occur as small signet-ring forms but occasionally as large rings, later becoming amoeboid and often extremely irregular. No dividing forms were seen either in the blood or in sections of spleen, liver, kidney, lung and intestine. The infected red cells showed no enlargement or stippling. The pigment is dark brown in colour and is very clearly seen in the microgametocyte. This form is characterized by its pale cytoplasm and large nucleus with deeply staining karyosome. Both sexes are slightly larger than the red cell, all trace of which disappears.

The infection appears to be of low pathogenicity, and it is noted that splenectomy failed to heighten the parasitaemia. The infection could not be transmitted by various species of *Anopheles*, *Culex*, *Armigeres* and *Aëdes* (*Stegomyia*) mosquitoes. Sub-inoculation of squirrel blood into laboratory animals and monkeys failed to cause infection.

The authors state that this parasite must be identical with that reported from the same locality by Donovan and named by him *P. ratufae* ; they point out that the morphology of the parasite of the Annam squirrel, *P. vassali*, Laveran 1905, is so similar, that a better provisional name for the Indian parasite would be *P. vassali* var. *ratufae*.

[It seems probable that this haemosporidian belongs to the same category as *H. kochi* of the African lower monkeys [this *Bulletin*, 1947, v. 44, 882], *Plasmodium* species of the Palestine bats (MER & GOLDBLUM, *Nature*, 1947, Mar. 29, 444), *P. pteropi* of the New Guinea flying foxes [MANWELL, this *Bulletin*, 1947, v. 44, 43] and *P. limnotragi* of the Citatunga [VAN DEN BERGHE, *Bull. Soc. Path. Exot.*, 1937, v. 30, 272]. Exo-erythrocytic schizogony has been described in the first three of these parasites—all in different forms ; its discovery in *ratufae* is awaited with interest.] *P. C. C. Garnham*

i. MARSHALL, P. B. **The Glucose Metabolism of** *Plasmodium gallinaceum*, **and the Action of Antimalarial Agents.** *Brit. J. Pharmacol.* 1948, Mar., v. 3, No. 1, 1–7, 2 figs. [16 refs.]

ii. ——. **The Glucose Metabolism of** *Trypanosoma evansi* **and the Action of Trypanocides.** *Ibid.* 8–14, 4 figs. [18 refs.]

i. The author has investigated the glucose metabolism of *P. gallinaceum* and the effect of antimalarial agents, on lines similar to those of the original

experiments of CHRISTOPHERS & FULTON [this *Bulletin*, 1938, v. 35, 709] and subsequent authors whose contributions have been regularly reviewed in this *Bulletin*. Infected blood from chickens containing 70 to 95 per cent. of parasitized cells suspended in isotonic buffer was used in Warburg manometers for the measurement of oxygen uptake. When required, accompanying glucose was removed by washing in the same buffer and the desired substrate or inhibitor added. Phosphorus exchanges were measured in these suspensions over periods of 4 to 5 hours during oxygenation. At the beginning and end of experiments, aliquots of suspensions were deproteinized and after centrifugation the supernatant was analysed for glucose, phosphorylated intermediates, lactic and pyruvic acids. In addition to glucose, washed parasitized red cells were able to oxidize glycerol, pyruvate, lactate and to a lesser extent succinate and fumarate. Cyanide and iodoacetic acid acted as inhibitors. Quinine and atebrin (mepacrine) did not appear to be active inhibitors of respiration, and differences in action were noted only at low concentrations of these drugs in presence of various substrates. Phosphorylation of glucose was more marked in parasitized than in normal red cells. The effect of inhibitors and antimalarial agents on phosphorylating reactions was also studied. The author's results did not agree with those of MOULDER & EVANS [this *Bulletin*, 1946, v. 43, 1118] in regard to the use of amino-acids as substrates by the parasite or the nitrogen exchanges brought about by it. A possible pathway for glucose metabolism, and mode of interference with it by quinine and mepacrine, is outlined.

ii. These experiments on the respiratory metabolism of *T. evansi* have in general confirmed the work of previous authors, including that of CHEN & GEILING (*Proc. Soc. Exper. Biol. & Med.*, 1946, v. 63, 486) who showed that phosphorylation reactions play a part in the metabolism of glucose by trypanosomes. The experimental methods were similar to those described above. Whole blood from mice infected with *T. evansi* was used, or in some cases suspensions of the parasite freed from red cells. The effect of a trivalent and a pentavalent arsenical, as well as of representative diamidines, on metabolism was investigated. The chief end-product of glucose utilization was pyruvic acid. In the case of trypanosomes freed from blood constituents, mouse plasma caused an increase in respiration possibly because of the presence of certain nutrient factors. When a number of such nutrients, including pantothenate, were added to suspensions, no increase in O_2 uptake was, however, observed. As in the case of other trypanosomes, glycerol was metabolized, but not lactate, fumarate, succinate, glutamate or aspartate. Iodoacetic acid and fluoride inhibited oxygen uptake but cyanide only to a slight extent. Trypanocides were active in this respect to varying degrees. Hexokinase is possibly inhibited by trivalent arsenicals. A scheme is outlined for the possible phosphorylation reactions involved during glucose metabolism by the trypanosomes.

[It is surprising to find in the first paper the statement that "Maier & Coggeshall (1941) showed that parasitized red cells were dependent to some extent on glucose, and that mannose, fructose and glycerol would replace glucose as a metabolite" since the American authors in the paper quoted, write "Fulton (1939) reported that if the blood glucose was removed from the parasite by washing, there was a decrease in respiration which could be restored to its former level by the addition of glucose. Fructose, mannose, maltose, or glycerol could be utilized as substitutes for glucose."] *J. D. Fulton*

TERZIAN, L. A. & SAXE, L. H. **The Effect of Oxygen Tension on *Plasmodium gallinaceum* Malaria in Chicks.** *J. Infect. Dis.* 1948, Jan.–Feb., v. 82, No. 1, 1–4, 1 fig.

"1. Exposure to oxygen at atmospheric and increased pressures for periods of 4 to 10 hours daily had no effect on the rate or degree of parasitemia, the

development of exo-erythrocytic forms, or the survival time of chicks infected with *Plasmodium gallinaceum*.

"2. Prolonged daily exposures to oxygen at atmospheric pressure, resulted in a significant decrease in survival time, accompanied during the later stages of the infection by inability of the treated birds to readjust to ordinary air.

"3. Oxygen administration, supplemented by quinine therapy, did not alter the course of the infection, and in most cases decreased survival time."

BELTRÁN, E. Estudio comparativo de dos plasmodios parasitos de la gallina domestica (*Plasmodium gallinaceum* y *P. juxtanucleare*). [**Comparative Study of** *P. gallinaceum* **and** *P. juxtanucleare*.] *Rev. Inst. Salubridad y Enfermedades Trop.* Mexico. 1947, June, v. 8, No. 2, 129–38, 1 map. [23 refs.] English summary.

The author compares the two malarial parasites of the fowl—*P. gallinaceum* described by BRUMPT in 1935, and *P. juxtanucleare* first recorded by VERSIANI and GOMES in 1941 [this *Bulletin*, 1942, v. 39, 400] from Brazil and by the author in the same year from Mexico. The former is a large parasite producing 24 merozoites and belongs to the Old World, while the latter is a small parasite giving rise to 4 merozoites. The data available for *P. juxtanucleare* are very incomplete, as it has been little investigated. *C. M. Wenyon*

MICKS, D. W. **A Loss of Gametocytes in** *Plasmodium elongatum*. *J. Parasitology*. 1947, Dec., v. 33, No. 6, 499–505, 2 figs. [12 refs.]

A strain of *P. elongatum* which had been maintained, since its isolation from a field sparrow, in canaries (10 passages) and ducks (10 passages) and which gave a parasite rate of 3·6 infected cells per 100 red corpuscles (90 per cent. of the parasites being gametocytes) was subinoculated to canaries. After 5 further passages of the duck strain (15 in all) and 4 passages of the canary strain, both strains became free from gametocytes. The two strains free of gametocytes were carried on through many duck and canary passages, but they never returned to normal. Inoculation to a sparrow produced no change. Two other strains started in ducks from canaries and the original canary strain ran a normal course. *C. M. Wenyon*

BLACKWATER FEVER

DAWSON, J. & FINDLAY, G. M. **Experiments on the relation of Haemoglobinuria and Anuria with reference to Blackwater Fever.** *Ann. Trop. Med. & Parasit.* 1947, Dec., v. 41, Nos. 3/4, 306–20, 9 graphs. [18 refs.]

This very interesting paper records the results of experiments designed to determine the effects of injection of haemoglobin or its derivatives in dogs and monkeys.

Injection of 3 gm. homologous haemoglobin depressed glomerular filtration rate (measured by inulin clearance) slightly in normal dogs and to a much greater degree in dogs which had been bled severely eighteen hours before the injection. The urinary flow was not affected in normal dogs; in the bled animals it was greatly diminished and in some cases ceased. Serial counts of "blocked" tubules in renal tissue showed there was no correlation between the extent of tubular blocking and the clinical result of the injection. On the other hand, the glomerular capillaries were empty in 78 per cent. of the bled dogs and

in only 32 per cent. of the normal animals. The authors concluded that impairment of the glomerular filtration and not blocking, was the basis of the interference with urinary flow, and that filtration was much more seriously affected in the animals which had been subjected to haemorrhage. The oliguria, anuria and reduction in inulin clearance were related to lack of blood supply to the glomeruli, as previously postulated by MAEGRAITH and FINDLAY [this *Bulletin*, 1945, v. 42, 12].

The effect of injection of haemoglobin on the blood pressure of dogs was measured directly and it was demonstrated that, whereas little change was observed in normal animals, in dogs which had previously been bled, a rise in blood pressure occurred after haemoglobin injection. This rise of blood pressure "could be correlated with the absence of blood from the glomerular capillaries." Further experiments showed that from 60 to 90 minutes after injection of haemoglobin into anaemic animals, a pressor substance could be extracted from the circulating blood. This substance was not present in blood from injected normal animals. Its production appeared in some way to be related to diminution of the oxygen-carrying power of the blood.

As a result of the chance observation that histidine output in the urine increased for 24 hours after transfusion in a case of toxaemia of pregnancy, the output of this amino-acid was estimated in cases of haemoglobinuria in Africans. No obvious correlation was noted between the output of histidine and haemoglobin. In one case of haemoglobinuria which was almost anuric, however, the histidine excretion was greatly increased during the period of lowest urinary output. Blood removed immediately after the death of this patient was extracted in the same way as the dog's blood and found to contain a pressor substance.

Working on the hypothesis that the pressor substance might be developed in a manner similar to angiotonin, which contains histidine, the authors attempted to prepare a pressor substance (pepsitensin) with the use of haemoglobin as a substrate and commercial pepsin as the enzyme. The pressor activity of the extract was not constant. If the extract had low free histidine content, it was active; if rich in histidine, it was inactive.

The authors suggest that failure of histidine excretion in a patient during intravascular haemolysis may be due to the development of some pressor substance in the blood. On the analogy of the renin-angiotonin system, renal anoxia (arising from anaemia) might promote the appearance of an enzyme capable of acting on the globin of haemoglobin to produce a pressor substance, possibly a polypeptide. This would constrict the glomerular vessels, increase the degree of renal anoxia and diminish the glomerular filtration rate.

B. G. Maegraith

HARRISON, H. E., BUNTING, H., ORDWAY, N. K. & ALBRINK, W. S. **The Pathogenesis of the Renal Injury produced in the Dog by Hemoglobin or Methemoglobin.** *J. Exper. Med.* 1947, Oct. 1, v. 86, No. 4, 339–56, 6 text figs. & 6 figs. (1 coloured) on 3 pls. [23 refs.]

This paper deals with the pathogenesis of renal dysfunction in dogs resulting (1) from intravascular haemolysis occurring after exposure to arsine gas, and (2) from intravenous injection of solutions of homologous haemoglobin and methaemoglobin. Kidney function was studied by serial estimations of blood urea N, plasma creatine and creatinine clearances; filtration of fluid through the glomerular membrane was determined by intravenous administration of ferrocyanide and subsequent examination of frozen kidney sections. Direct measurement of renal venous flow was made in two dogs in which one kidney was brought to the flank under anaesthesia "without tension on the pedicle."

Dogs were found to be resistant to the injurious effects of intravascular haemolysis after exposure to arsine ; renal injury was apparent only in cases of extreme haemolysis. Injection of solutions of haemoglobin affected renal function only when the dosage was large. Small doses of haemoglobin injected into four animals made oliguric by deprivation of water caused no appreciable change in plasma urea N. Larger doses in oliguric dogs produced temporary anuria and changes in endogenous creatinine clearance.

The authors quote BING's results (*Bull. Johns Hopkins Hosp.*, 1944, v. 74, 161) which showed that severe renal injury followed injection of methaemoglobin in dogs rendered acidotic with ammonium chloride, whereas injection of methaemoglobin or comparable amounts of haemoglobin in normal animals had little effect. They determined the effects of injection of methaemoglobin in normal dogs, dogs made oliguric by deprivation of water, and dogs rendered " acidotic " by intragastric injection of 0·1 N hydrochloric acid.

In non-acidotic dogs with good urinary flow, injection of methaemoglobin in doses of 1 gm. per kilo. had no effect on renal function. The same dosage in oliguric non-acidotic dogs had serious effects in some cases, including temporary or permanent anuria. In acidotic dogs, in which the urinary output was high, injection of methaemoglobin appeared to have little deleterious effect ; in the one animal for which details are given, it produced a temporary diuresis. The authors conclude that in these acidotic animals " although acidosis probably did have some effect in increasing the kidney damage . . . the rate of urine flow was the more important."

Creatinine clearances were measured in some dogs before and after injection of haemoglobin and methaemoglobin. Representative figures are given in text tables.

Injection of haemoglobin in doses of about 4 gm./kilo. into two oliguric dogs produced immediate almost complete stoppage of urinary flow. In one animal, this period of anuria was of short duration and was followed by a great increase of urinary flow, up to seven times greater than during the original oliguric state ; twenty hours later, the urinary flow was still twice what it had been before injection. Endogenous creatinine clearance was reduced in this dog to two-thirds 60 minutes after the injection and to one-half of the initial figure twenty hours later. In the second dog, there was no post-anuric diuresis and the urinary flow was about double the initial flow twenty hours after the injection ; creatinine clearance fell to a trace after the injection and twenty hours later was still only one-sixtieth of the original level.

Injection of methaemoglobin in doses of about 1 gm./kilo. into two oliguric dogs produced anuria in both. This persisted in one animal, but in the other urinary flow was restored to the pre-injection level after 90 minutes. In the anuric dog, the creatinine clearance was reduced to a trace. In the other animal, it fell to about one-fiftieth of the original figure about 100 minutes after the injection and was only one-eighteenth four hours later, although the urinary flow had been re-established.

In the one acidotic dog for which details are given, the same dose of methaemoglobin produced a diuresis associated with a reduction of creatinine clearance in the first hour after injection. Subsequently the urinary flow continued at a slightly greater rate than before the injection, but the creatinine slowly fell to one-fifth of the initial figure.

It will be seen from these figures that there appeared to be little relation between the prevailing urinary flow and the endogenous creatinine clearance. Nevertheless, the authors considered the possibility that " a marked reduction of renal blood flow " occurred after the injection of the pigments. They measured renal venous flow directly in two oliguric animals injected with a dose of 1 gm. methaemoglobin per kilo. No evidence of reduction of (total)

renal blood flow was found in either animal except after " prolonged anaesthesia and manipulation."

Histological changes in the form of eosinophilic granular precipitates in the glomerular spaces and lumina of the tubules were found within a few hours of the onset of haemoglobinuria in dogs exposed to arsine or injection of haemoglobin or methaemoglobin. With 24 hours of exposure to arsine and two hours after injection of the pigments " masses of granular yellow-brown refractile material and well-formed casts " were found in the loops of Henle, distal convoluted tubules and collecting tubules. In severe cases of haemoglobinuria, hyaline eosinophilic droplets which the authors considered to be haemoglobin were found in the epithelium of the proximal convoluted tubules. By 36 to 48 hours after the onset of haemoglobinuria, coagulative necrosis of the epithelium of some of the proximal convoluted tubules was evident. Later, signs of regeneration of epithelium appeared and granules containing free iron were found in the epithelial cells. After 3 or 4 days " radial zones of tubules containing casts, alternating with sections free of casts "(often with dilated tubules) were seen. Injection of ferrocyanide showed that filtration through the glomerular membrane had occurred even in apparently blocked tubules. The material filling the lumina of the tubules was identified as mainly methaemoglobin " in concentrated solution of gel-like consistency." The number of casts per unit area of cortex and medulla was determined. The degree of impairment of renal function was greatest in those animals in which casts were most numerous, and least in those in which casts were few. In four animals, renal insufficiency was present in association with " only a small number of casts ", and in these no " anatomical " basis for impaired function was found.

The authors conclude that " severe and persistent impairment of kidney function " results in dogs from intravascular haemolysis after exposure to arsine and from intravenous injection of solutions of homologous haemoglobin and methaemoglobin. They consider the evidence presented in their paper shows that obstruction to urinary flow through the tubules is " an important factor in the early reduction of kidney function ". The material in the lumina was a concentrated solution of methaemoglobin and there was no evidence of the formation of pigment insoluble at the *p*H of urine (after methaemoglobin injection, the *p*H of the urine *rose* in some animals at the beginning of haemoglobinuria). Injury to the epithelium of the proximal convoluted tubules occurred late after injection of methaemoglobin, haemoglobin or following exposure to arsine. Such epithelial damage probably contributed to the persistent severe depression of renal function.

Direct measurement of renal venous flow in two dogs did not confirm the observation of other workers who held that injection of haemoglobin caused a reduction in renal blood flow. (In these experiments the authors injected methaemoglobin.)

[In coming to their conclusions, the authors have had the advantage over the reader in that they have had access to all the protocols of experiments. The information provided in the text is often inadequate. For instance, the table illustrating the correlation between the number of casts, histological changes in the proximal tubules and evidence of impairment of renal function, gives no indication of the dose of arsine or methaemoglobin used. It is thus not possible to see what relation existed between the dose and the severity of the lesion, which considerably weakens the argument. Similarly, the evidence provided concerning changes in creatinine clearances is insufficient and inadequate from the point of view of the conclusions drawn. In the experiments quoted in the tables, there appears to be little relation between rate of urinary flow and the changes in creatinine clearance. The acknowledgment that the urinary flow was an important factor in modifying the effects of methaemoglobin injection

in acidotic dogs, might be a useful argument in favour of the view that the pathogenesis of renal injury of this kind is related to the glomerular blood flow.

The two experiments in which renal blood flow were measured show a reduction in total flow some time after the injection of methaemoglobin, in one case after the re-establishment of oliguric flow, in the other during anuria. It is possible to interpret these results as the authors have done, provided the surgical interference and transposition of the kidneys is disregarded, in terms of no reduction in renal flow following the injection. It should be noted, however, that this refers only to total flow and has no reference to the flow through the cortex, which, for all the evidence provided here, may as well be shunted to the medulla as not. This paper leaves us much where we were.]

B. G. Maegraith.

KHO LIEN KENG. Een geval van zwartwaterkoorts met cyanose (methaemoglobinaemie), waarschijnlijk door plasmochine. [**Blackwater Fever and Cyanosis of Plasmoquine Origin.**] *Med. Maandblad.* Batavia. 1948, Jan., No. 18, 342–7. [30 refs.]

Plasmoquine has certain advantages by its gametocidal action in malaria therapy, but is undoubtedly toxic. The problem of the cause of blackwater fever is linked in the literature with malaria, quinine and plasmoquine. It is now more than twenty years since plasmoquine was announced (1926) as a drug for use and, in the light of what is now known of its toxic character, it is astonishing to learn that, originally, it was given in a dose of even 250 mgm. daily. The present article gives a useful historical account of the subject as introduction to the author's own case of blackwater fever with cyanosis (methaemoglobinaemia). The patient was a young Chinese of 17 years who came for consultation with fever which had started the day before. It was not surprising that, as he lived in Batavia and suffered regularly from 3 to 4 attacks of malaria every year, a blood film showed the presence of tertian malaria schizonts. He was given a prescription for 300 mgm. quinine bisulphate four times daily for five days and the temperature fell immediately. Five days after stopping treatment the fever, in this subject of chronic malaria, recurred and he was now given 300 mgm. quinine together with 10 mgm. plasmoquine, both three times daily. Four days later he reappeared still with fever, looking cyanotic and passing dark red urine. Other symptoms were vomiting, headache, cough and general malaise but no enlargement of the spleen. The blood serum was dark brown and gave the spectrum of methaemoglobin only, oxy- and sulphaemoglobin being excluded. There was no direct van den Bergh reaction, but the indirect reaction was obtained on two occasions. After the patient's admission to hospital, the haemoglobinuria lasted 3 days, the cyanosis a week and jaundice 10 days. His temperature fluctuated between 102° and 105·8°F. and he was occasionally delirious. A thick blood film showed no parasites. No albumin, no sugar, but much urobilin were present in the urine. Treatment consisted of vitamins, fruit and fluid. Diuresis was good. A blood transfusion of 250 ml. was followed by a pyrexial reaction.

Differential diagnosis lay between blackwater fever and plasmoquine toxaemia. "It is not improbable that sensitization by previous malarial attacks and plasmoquine poisoning are contributory to the development of blackwater fever."

W. F. Harvey

TRYPANOSOMIASIS

McLETCHIE, J. L. **The Control of Sleeping Sickness in Nigeria.** *Trans. Roy. Soc. Trop. Med. & Hyg.* 1948, Jan., v. 41, No. 4, 445–70, 4 maps & 9 figs. [35 refs.] Discussion 471–80 [HOLLINS, C.; TODD, K. W.; RAE, Wilson; DUGGAN, A. J.; BUXTON, P. A.; CHESTERMAN, C. C.; MACDONALD, G.; MANSON-BAHR, P.; McLETCHIE (in reply)].

The author has divided his account of the control of sleeping sickness in Nigeria into several parts: the distribution of tsetse flies, drug resistance of trypanosomes, incidence of the disease, characters of the disease, treatment, prophylaxis and control. The paper, therefore, contains more than its title indicates, and is, in fact, a very comprehensive statement of the whole position, written by a man who has been very actively implicated in the work.

The earlier sections of the paper are themselves largely accounts of work done and opinions expressed by other people. The vectors are *Glossina palpalis* and *G. tachinoides*, the trypansome is *T. gambiense*, which gives rise to three categories of disease: mild and scanty blood infection; moderately virulent, invading the nervous system in 6–12 months; severe (like the Rhodesian form) but only feebly transmissible. These have been described before by LESTER.

In Nigeria and other West African countries, sleeping sickness was considered to be quiescent and sporadic before 1925, but about that time there occurred a great increase in incidence, which was due, not to the spread of tsetse, but to dispersal and free movement of the population. Survey teams were organized in 1930, and in the first five years found an incidence of 13·6 per cent. in 1¼ million persons examined. In some places the rate was up to 20 per cent. In the next five years, the extent of the infected areas was more clearly defined, and the average incidence was 8·6 per cent. In the last period—of 6 years—the incidence in new surveys was 1·5 per cent.

McLetchie stresses the point made by several authors, that even in areas in which the type of sleeping sickness is apparently mild, and in which the infected persons appear to be in good health, the death rate is high. The mild disease may be only slowly progressive as regards involvement of the nervous system, but sudden breakdown, with high fever and toxaemia, occurs and is, apparently, relatively common. The trypanosome of low virulence is specially associated with epidemics, being easily transmissible. On the other hand, true mild cases do occur, in which infection persists for years, the patient and the parasite being in a state of equilibrium.

Treatment varies according to conditions, but a combination of antrypol (0·5 gm.) and tryparsamide (1·5 gm.) is becoming more common. This combination is given at intervals of 5 days, for 6–20 injections according to severity. Pentamidine (intramuscularly) can replace antrypol, and can be given at the same time as tryparsamide. One intensive course, for use in small remote groups, consists of pentamidine isethionate 100 mgm. the first day, followed by 200 mgm. daily to the seventh day, together with tryparsamide injections to a total of 6–9 gm. in the same seven days, or in ten days. Pentamidine is also used as a prophylactic.

In control, the first step has been mass treatment, and this was essential in the face of epidemics. Since 1931, half a million patients have been treated, most during surveys and at dispensaries, but over 50,000 at general medical stations. The incidence rate in populations examined, which rose to 20·5 per cent. in 1935, was in 1945 down to 1·2 in new surveys. The dispensaries are popular.

Control of tsetse comprises protective clearing of streams (rod clearings), and aggressive clearing of large areas. Of the latter, the Anchau corridor is

the most ambitious example ; it is briefly described in the present paper, on the lines of the previous description given by the author [see this *Bulletin*, 1946, v. 43, 1022]. The basic policy for control in Nigeria is mass treatment, dispensary follow-up, and clearance by communal effort. The effect of insecticidal methods has not yet been investigated on a large scale. *Charles Wilcocks*

VAUCEL, M. & CECCALDI, J. Les anciens trypanosomés se réinfectent-ils ? [**Do Former Patients with Trypanosomiasis become infected a Second Time ?**] *Liber Jubilaris J. Rodhain* (*Soc. Belge Méd. Trop., Brussels*). 1947, Dec., 395–409. [10 refs.]

Four patients are described who were discovered during a routine examination to be infected with trypanosomes. Their general clinical condition was good and there was no evidence of infection of the nervous system. They were treated with atoxyl, tartar emetic or Fourneau 270 and followed up by examinations every 6 months. After 8 to 12 years they were found to be infected once again, but the infections responded readily to the usual treatments. Three other patients, who had applied for treatment owing to their symptoms, were treated with atoxyl-tartar-emetic, tryparsamide or Fourneau 270. Five to eight years later, they were found to be infected again ; they responded readily to further treatment. The interpretation of these cases is discussed. Five or more of the patients may have been reinfected. On the other hand, all the cases may represent reactivation of the infection after a prolonged latent period. The evidence is insufficient to decide which of these interpretations is correct.

F. Hawking

BUCK, Margaret. **Persistence of the Parabasal Body in a *p*-Rosaniline Resistant Strain of *Trypanosoma brucei*.** *Proc. Soc. Exper. Biol. & Med.* 1948, Jan., v. 67, No. 1, 77–9, 1 fig.

" A *p*-rosaniline-resistant modification of *T. brucei* is described in which—contrary to the experience with other trypanosome strains—the parabasal body persisted. The strain also failed to show the overlapping resistance to 6,6′-ureylene [4-amino-2-methyl-quinoline] which could be demonstrated in *p*-rosaniline-fast strains of *T. equiperdum*."

VAN HOOF, L., HENRARD, C. & PEEL, E. Observations sur le *Trypanosoma brucei* produisant des infections naturelles dans une région infestée de *Glossina palpalis*, en l'absence de *G. morsitans*. [**Observations on *T. brucei* producing Natural Infections in a *Glossina palpalis* Region, in the absence of *G. morsitans*.**] *Liber Jubilaris J. Rodhain* (*Soc. Belge Méd. Trop., Brussels*). 1947, Dec., 359–80, 3 figs. [11 refs.]

Description of three strains of *T. brucei*, from natural infections in a dog, pig and goat, isolated in the western region of the Belgian Congo, where the only important vector is *Glossina palpalis*. With these strains cyclical and mechanical passages were carried out through various mammals, including man.

Both in natural and experimental infections of pigs, *T. brucei* was more abundant in the blood than in the case of *T. gambiense* infections, the number of parasites gradually diminishing until the animals recovered spontaneously after periods up to 15 months. Attempts to reinfect the pigs with *T. gambiense* failed but were successful with *T. rhodesiense*. It is suggested that in *palpalis* areas the pig probably serves as a reservoir of *T. brucei*. In goats, *T. brucei* produced acute or subacute infections, terminating fatally in from one to seven months, with symptoms of encephalitis. In dogs the infection ran an acute or subacute course, with the characteristic symptoms of keratitis, on account of

which the dog may serve as a test-animal for differentiating *T. brucei* from the human trypanosomes. The behaviour of *T. brucei* in monkeys varied: while the susceptibility of *Cercocebus* was low, the infection running a symptomless course with spontaneous recovery, *Cercopithecus* was highly susceptible, the course of the disease being acute and fatal.

The index of transmissibility of the porcine and caprine strains of *T. brucei* by *G. palpalis* was higher than that of *T. gambiense*. It was found that passage through *Cercocebus* considerably increased its transmissibility. Tsetse-flies fed on cultures maintained for 6 months became infected and were able to transmit the infection cyclically to guineapigs.

Since a chronic infection correlated with a high degree of transmissibility is an ideal condition for the maintenance of endemicity, it is thought that in the region under consideration, where game is scarce, the best reservoir host of *T. brucei* is provided by the pig.

Treatment with various drugs showed that *T. brucei* was fairly resistant to tryparsamide, about 0·3 gm. per kgm. being required to effect a cure in guinea-pigs. As regards tartar emetic, 3 injections of 0·05 gm. was the curative dose for dogs, while guineapigs required 1 mgm. per kgm. combined with 0·005 gm. per kgm. of Bayer 205; the latter drug produced the best results in doses of 0·05 gm. per kgm. against all three strains; on the other hand, Surfen C was ineffective.

Normal human serum had a pronounced trypanocidal action on all three strains of *T. brucei*, 3–6 cc. causing the disappearance of the trypanosomes from the blood in guineapigs, while 1 cc. had a prophylactic effect. This trypanosome was made serum-resistant by administering progressively increasing subcurative doses, until resistance to 100 cc. was produced in guineapigs.

The pathogenicity of *T. brucei* to man was tested by cyclical transmission to seven volunteers of the canine and caprine strains, from the natural hosts, after passages through domestic animals, and after rendering the trypanosomes resistant to human serum. All these attempts, except one, failed. In the positive case trypanosomes were seen in a thick blood film of the volunteer three weeks after the infective bites by tsetse, but subsequent examinations of the blood and cultures were negative, and inoculation of the blood to other animals produced no infection.

The human experiments were designed to elucidate the rôle of *T. brucei* in the genesis of acute cases of sleeping sickness of the *rhodesiense* type which occur in *gambiense* areas in the presence of *G. palpalis* vectors. The single positive case represents a transient infection in a person who was exceptionally susceptible to the infection. The authors suggest that among numerous persons exposed to the bites of tsetse-flies infected with *T. brucei*, the susceptibility of some individuals might occasionally be still greater, the infection lasting long enough to allow the flies to feed, acquire an infection and transmit it further. In this way there might be produced a mutant strain of *T. brucei* which would adapt itself to the new host.

The existence of cross-immunity between *T. brucei* and *T. gambiense* points to the presence of group antigens in the polymorphic trypanosomes. It is suggested that the relationship between these trypanosomes could be tested by attempting to transform *T. gambiense* into *T. brucei* virulent to dogs or goats. *C. A. Hoare*

HOARE, C. A. **Tsetse-borne Trypanosomiases outside their Natural Boundaries.** *Liber Jubilaris J. Rodhain* (*Soc. Belge Méd. Trop., Brussels*). 1947, Dec., 267–77. [26 refs.]

It has been shown experimentally that pathogenic trypanosomes of man and animals in Africa which are cyclically transmitted by tsetse flies can also be

conveyed mechanically by other biting flies, particularly tabanids, when the time between two successive bites is very short; there is little doubt that this occurs in herds of animals in tsetse-free areas of Africa though, as these are situated near to tsetse-infested areas, the long establishment of infection by mechanical transmission alone is difficult to prove. In countries far from Africa, however, such as Mauritius, the West Indies, Central America and South America, where no tsetse flies exist and where infection with *Trypanosoma vivax* among domestic animals has become a serious problem, it must be concluded that the disease is spread by mechanical transmission by biting flies. Other tsetse-borne pathogenic trypanosomes, imported into tsetse-free areas, have caused outbreaks of disease in animals, but the infections have not become established there.

These facts arouse interest in the question of the relationship of *T. brucei* to *T. evansi*; the latter is monomorphic and indistinguishable in appearance from the long, thin forms of *T. brucei*, but some strains of *T. evansi* show polymorphism and even posterior-nuclear forms, yet in experiments they failed to infect tsetse flies. Laboratory strains of *T. brucei*, maintained by syringe-passage, eventually become monomorphic, the long, thin forms alone persisting, and lose their power of developing in tsetse flies. It was found also that strains of *T. vivax* in tsetse-free countries (Ruanda and Martinique) could not develop in tsetse flies. It is suggested, therefore, that *T. evansi* has arisen from *T. brucei*; camels may have been infected with *T. brucei* during visits to tsetse-infested areas and on their return to the Sudan the infection was spread mechanically by tabanids, became established and was carried in caravans to Asia and elsewhere. An alternative suggestion that *T. brucei* was originally *T. evansi* cannot be excluded. [The articles in the list of references have nearly all been abstracted in this *Bulletin* from 1930 onwards.] *J. F. Corson*

HOPPE, J. O. & CHAPMAN, C. W. **Rôle of Glucose in Acute Parasitemic Death of the Rat infected with** *Trypanosoma equiperdum*. *J. Parasitology*. 1947, Dec., v. 33, No. 6, 509–16, 1 fig. [19 refs.]

Rats infected with *T. equiperdum* by intraperitoneal injection of 2 million trypanosomes survived 90·65 ± 34 hours. During the infection, the blood sugar decreased from a normal of 145·6 milligrammes per cent. to 32·8 milligrammes per cent. at the time of death. The sugar remained at the normal level for the first 48 hours, then decreased by 1 per cent. per hour up to 72 hours and finally by 3 per cent. per hour to the death of the animal. At the time of death, the trypanosomes numbered 1·566 million per cmm. of blood. If 5 gm. of glucose per kgm. of body weight was administered orally every three hours, commencing shortly before the expected death of the rat, life would be prolonged on an average 18 hours, the trypanosomes reaching 3·744 million per cmm. of blood. The rats at 48 hours of the infection survived doses of insulin not greater than 5 units per kgm., while normal rats survived 400 units per kgm. From the authors' observations, the conclusion is reached that hypoglycaemia is the cause of death in albino rats infected with *T. equiperdum*. *C. M. Wenyon*

See also p. 495, MARSHALL, **The Glucose Metabolism of** *Trypanosoma evansi*, **and the Action of Trypanocides.**

CHEN, G. & MCCREARY, J. H. **An Evaluation of Assay Methods for Arsenicals.** *J. Pharm. & Exper. Therap.* 1947, Oct., v. 91, No. 2, 140–43, 1 fig.

Chen *et al.* previously described an *in vivo* and an *in vitro* method for the assay of trypanocidal activity of antimonials [this *Bulletin*, 1945, v. 42, 869;

1946, v. 43, 315]. The former was based on the suppressive and curative activity of the drugs in *T. equiperdum* infections of mice and the latter on the interference with glucose metabolism of the isolated trypanosomes. Similar methods have now been used for evaluating arsenicals. In addition, the concentration of various drugs which caused death of the trypanosomes over an observation period of one hour was determined in coverslip preparations of infected blood mixed with Ringer-Locke solution. The results obtained by the two *in vivo* methods agreed well among themselves and also with those based on interference with glucose metabolism in the case of tervalent compounds. When potencies were estimated by comparing lethal concentrations of the substances in coverslip preparations, the results were not in harmony with those of the other tests. The authors consider that the suppressive method of estimating trypanocidal potencies of arsenicals is satisfactory. The *in vitro* method, based on interference with glucose metabolism by the trypanosomes, has advantages for certain classes of arsenicals on account of its simplicity.

J. D. Fulton

FLOCH, H. La maladie de Chagas en Guyane française. [**Chagas's Disease in French Guiana.**] *Institut Pasteur de la Guyane et du Territoire de l'Inini. Publication No. 164.* 1947, Nov., 5 pp. [13 refs.]

FLOCH, H. & CAMAIN, R. Deux nouveaux cas de maladie de Chagas en Guyane française. [**Two New Cases of Chagas's Disease in French Guiana.**] *Institut Pasteur de la Guyane et du Territoire de l'Inini. Publication No. 162.* 1947, Sept., 4 pp.

PELLEGRINO, J. & MESQUITA, S. S. A reação de fixação do complemento na doença de Chagas. I—Nota sôbre falsas reações positivas e duvidosas feitas com antígeno de cultura de "Schizotrypanum cruzi" em sôros conservados em geladeira. [**Complement Fixation in Chagas's Disease. I. False and Doubtful Positives with Culture Antigen.**] *Brasil-Medico.* 1947, Nov. 22 & 29, v. 61, Nos. 47/48, 396–401. [13 refs.] English summary.

Diagnosis of Chagas's disease in the early stages, when *T. cruzi* is abundant in the blood-stream, is a simple matter; later we have to rely more on xenodiagnosis, inoculation and cultivation. Such methods, especially xenodiagnosis, are lengthy and not always certain. Hence the value of the Guerreiro-Machado reaction in these stages with suspensions of trypanosomes from the blood of infected animals [see this *Bulletin*, 1928, v. 25, 356; 1938, v. 35, 721]. The authors in this study have used a culture of *T. cruzi* prepared by DAVIS's method [*ibid.*, 1943, v. 40, 890] slightly modified by MUNIZ and FREITAS [*ibid.*, 1945, v. 42, 975; 1947, v. 44, 571]. They found that sera of some persons, apparently in good health, with no signs of infection, gave doubtful and even in some (though not many) cases positive complement-fixation if the sera had been kept in an ice-chest, even with addition of merthiolate. To avoid this error, the reaction must be carried out with freshly obtained serum. The results are shown in protocols.

H. Harold Scott

LEISHMANIASIS

HAWKING, F. **Growth of Protozoa in Tissue Culture. V.** *Leishmania donovani. Trans. Roy. Soc. Trop. Med. & Hyg.* 1948, Jan., v. 41, No. 4, 545–54, 23 figs. (2 coloured). [15 refs.]

The author has succeeded in cultivating *Leishmania donovani* in tissue culture, employing hamster spleen as the tissue and rabbit serum in the liquid portion

in place of hamster serum. In cultures made from infected spleens, active multiplication of parasites occurred and these were able to invade uninfected spleen growing in the same Carrell flask. In most of the cultures maintained for more than sixteen days the parasites escaped from the cells and formed masses of flagellates which grew and multiplied at 37°C. Cultures of flagellates growing at 25°C. were added to culture of hamster spleen growing at 37°C.; some of the flagellates entered cells and appeared as leishmania forms, while other flagellates multiplied in the fluid part of the medium. *C. M. Wenyon*

AVERSA, T. & CROSCA, A. Modificazioni del quadro ematologico e del mielogramma sotto l'influenza della terapia abbinata di ferro e di antimonio nella leishmaniosi interna infantile. [**Changes in the Blood Picture and the Myelogram as a Result of Combined Iron and Antimony Treatment in Infantile Kala Azar.**] *Pediatria.* 1947, v. 55, Nos. 10/12, 607–21.

The English summary appended to the paper is as follows :—.

" The authors have studied the changes of the blood-picture and myelogram under the influence of combined iron- and antimony therapy, in 9 children affected by visceral leishmaniasis.

" The improvement of the blood-picture was neither more rapid nor more accentuated than that we generally observe in children treated only with antimony.

" Likewise the medullary alterations were not differently modified."

BURGIO, G. R. Rilievi statistico-clinici sull'endemia del kala-azar nostrano nella Sicilia occidentale negli anni 1939–1945. [**Infantile Kala Azar in Western Sicily.**] *Pediatria.* 1947, v. 55, Nos. 1/3, 53–80, 9 graphs & 1 map. [30 refs.] English summary.

Basing his observations on children in Palermo seen at the pediatric clinic, in the children's hospital or attending its out-patient department, the author finds that the cases of kala azar have remained fairly constant, the numbers for 1939 to 1943 being 26, 27, 26, 33, 18. In 1944 and 1945, however, there was a marked increase, the figures 80 and 84 being obtained. This increase was due largely to the cases from the Palermo district. *C. M. Wenyon*

CARNEVALE, A. La velocità di diffusione di un elettrolita (HCl), nel gel-serico, nella leishmaniosi interna. [**Diffusion Speed of an Electrolyte in Frozen Kala Azar Serum.**] *Pediatria.* 1947, v. 55, Nos. 1/3, 81–6. English summary (7 lines).

The author has found that an electrolyte (HCl) diffused more rapidly in serum gel of 14 of 15 cases of infantile kala azar (the normal rate being 44–47 mm. in 24 hours). This increase to 48–51 mm. appears to be related to the alteration which occurs in the albumin/globulin relationship, the globulin being increased in kala azar. In 7 healthy children, a rate of 45 or 46 was obtained. The technique, which consists essentially of gelification of the serum with propionic acid, and then adding a layer of HCl and observing penetration of the latter by colour change in Congo red previously incorporated, is described.

C. M. Wenyon

GUIMARÃES, F. N. Visceralisação da "Leishmania brasiliensis" Vianna, 1911, em hamsters ("Cricetus auratus"). (Nota preliminar.) [**Visceral** *L. brasiliensis* **Infection in Hamsters** (*Cricetus cricetus*=*C. auratus*).] *Brasil-Medico.* 1947, Nov. 22 & 29, v. 61, Nos. 47/48, 395–6, 2 figs.; Dec. 20 & 27, Nos. 51/52, 439 (Erratum).

With material taken from a sore containing leishmania, the author inoculated a hamster on the nose and in the peri-ocular region. Seven months later the animal was examined. There were no cutaneous lesions, but there was a generalized leishmania infection which is illustrated by photographs of a section of the spleen and a smear of the bone marrow. This appears to be the first record of a generalized infection with *Leishmania brasiliensis*. Similar infections have been produced by a number of observers with *Leishmania tropica*. In the second note, the name of the hamster is corrected to *Cricetus auratus* from *Cricetus cricetus*. *C. M. Wenyon*

FULTON, J. D. **The Constitution of Photostilbamidine, the Irradiation Product of Stilbamidine.** *Brit. J. Pharmacol.* 1948, Mar., v. 3, No. 1, 75–9, 2 figs. [16 refs.]

"Irradiation of a solution of *trans*-stilbamidine in sunlight gave a substance which on hydrolysis to the corresponding acid, followed by decarboxylation, yielded a hydrocarbon m.p. 163° identical with that obtained by irradiation of stilbene. The hydrocarbon previously described as di-stilbene has now been shown by *x*-ray crystallographic analysis to be 1 : 2 : 3 : 4-tetraphenyl-*cyclo*butane, containing a centre of symmetry. A second isomeric hydrocarbon m.p. 149° was also obtained in the same series of reactions, but its molecular configuration has not yet been determined. The isolation of these two hydrocarbons is in agreement with the view that stilbamidine undergoes dimerization on irradiation of its solutions." [See this *Bulletin*, 1947, v. 44, 988.]

FEVERS OF THE TYPHUS GROUP

JADIN, J. & D'HOOGHE, M. La fièvre rouge congolaise peut être aussi du typhus historique. [**Cases of Historic Typhus also may be included under the Name Red Fever of the Congo.**] *Liber Jubilaris J. Rodhain* (*Soc. Belge Méd. Trop., Brussels*). 1947, Dec., 279–90, 2 charts. [10 refs.]

Jadin has already isolated strains of murine-typhus rickettsiae from patients regarded as suffering from the red fever of the Congo. [See this *Bulletin*, 1948, v. 45, 323.]

The authors now claim to have isolated strains of epidemic-typhus rickettsiae from three out of eight patients in whose cases the same diagnosis was made.

The features said to be characteristic of the disease are fever, headache, rash, and a Weil-Felix reaction of the *Proteus OXK* type.

Six of the eight patients whose cases are described in the present paper reacted with *Pr. OXK* at titres of 1–200 or over, three also reacted with *Pr. OX2* at 1–100 or 1–200, and another with *Pr. OX19* at 1–2,000.

[There seems to be no valid reason for retaining the name *fièvre rouge congolaise* for fevers shown to belong to the typhus group.]

John W. D. Megaw

GREIFF, D. & PINKERTON, H. **Effect of Enzyme Inhibitors and Activators on the Multiplication of Typhus Rickettsiae. III. Correlation of Effects of PABA and KCN with Oxygen Consumption in Embryonate Eggs.** *J. Exper. Med.* 1948, Mar. 1, v. 87, No. 3, 175–97, 2 figs. [28 refs.]

This paper is the third of a series by the same authors. [See this *Bulletin*, 1945, v. 42, 362, and 1946, v. 43, 22.]

Using a special technique, which is described in the paper, the authors found that the rate of uptake of oxygen by eggs containing developing chick embryos became slightly increased on the fourth day after inoculation with rickettsiae and then fell rapidly during the later days.

PABA (para-aminobenzoic acid) introduced as described in the earlier papers caused a pronounced increase in the oxygen intake of the infected eggs, whereas MABA (meta-aminobenzoic acid) and OABA (ortho-aminobenzoic acid) caused a moderate degree of depression in the intake.

The small doses of potassium cyanide which had been found to enhance rickettsial growth, caused a striking depression in the oxygen intake.

These experiments are regarded as supporting the hypothesis that rickettsial growth is inversely proportional to the respiratory rate of the host cells.

Although PABA forms part of the folic-acid molecule, the latter drug in tolerated doses did not increase the oxygen uptake and had no rickettsiostatic action.

John W. D. Megaw

BHATTACHARJYA, B. **Clinical Features of Murine Typhus.** *Indian Med. Gaz.* 1947, Sept., v. 82, No. 9, 514–16, 4 charts.

A report of seven cases.

LANTIN, P. T., GAMBOA, E. L. & GERONIMO, A. **Endemic Typhus with Report of Cases.** *Santo Tomas J. of Med.* Manila. 1947, Nov., v. 2, No. 6, 293–300.

Describes two cases from Manila.

KALRA, S. L. **Scrub Typhus: Variations in Clinical Symptoms and Strains.** *Indian Med. Gaz.* 1947, Sept., v. 82, No. 9, 516–17.

The author presents evidence to show that scrub typhus, even in different parts of the same country, may vary greatly in severity. The fatality rates tend to fall into two groups, in one of which they are below 3 per cent. while in the other they are 8–10 per cent.

By inoculation experiments on the eyes of rabbits, he found that the rickettsial strains from different areas did not always immunize against each other.

John W. D. Megaw

HUEBNER, R. J., JELLISON, W. L., BECK, M. D., PARKER, R. R. & SHEPARD C. C. **Q Fever Studies in Southern California. I. Recovery of *Rickettsia burneti* from Raw Milk.** *Pub. Health Rep.* Wash. 1948, Feb. 13, v. 63, No. 7, 214–22.

The circumstances leading up to the present investigations are stated to have been that studies not yet published had indicated: (1) that 117 cases of Q fever had occurred in South California during 1947; (2) that more than half the patients had been workers in dairies or residents in places close to dairies; and (3) that 10–20 per cent. of the dairy cows of the Los Angeles area had given positive complement-fixation reactions with Q fever antigen.

The authors give details of the very thorough investigations carried out by them at the U.S.A. National Institute of Health, the Q Fever Laboratory, and

Rocky Mountain Laboratory, at all three of which similar results were obtained from the examination of the same samples of milk. Fifty samples of milk were obtained from four dairies, in association with which cases of Q fever had occurred. Most of the samples consisted of pools of milk each of which was obtained from 25–30 cows, but a few were from individual cows. Each sample was tested by guineapig inoculation, and from 40 of them evidence of Q fever infection was obtained in the form of complement-fixation reactions against Q fever antigens. Most of the reacting guineapigs had febrile reactions, and from eight of these, which were sacrificed, strains of *Rickettsia burneti* were isolated by further guineapig inoculation and by yolk-sac culture.

Each of several strains that were tested for cross immunity against known strains of *R. burneti* gave positive results.

None of the infected cows showed any signs of illness or of diminution in the yield of milk. The available evidence did not suggest that infection was transmitted to human beings by drinking milk, though it was considered possible that milk might be a source of infection by some mode yet to be determined.

John W. D. Megaw

YELLOW FEVER

WADDELL, Mary B. & TAYLOR, R. M. **Studies on Cyclic Passage of Yellow Fever Virus in South American Mammals and Mosquitoes. IV. Marsupials (*Metachirus nudicaudatus* and *Marmosa*) in combination with *Aedes aegypti* as Vector.** *Amer. J. Trop. Med.* 1948, Jan., v. 28, No. 1, 87–100, 5 figs. [14 refs.]

The authors have found that under appropriate conditions in the laboratory, certain strains of jungle yellow fever virus may be maintained in cyclical passages through marsupials (*Metachirus nudicaudatus* and *Marmosa cinerea*) in combination with *Aëdes aegypti* as the insect vector, and that strain differences of the virus may be of such magnitude as to affect their cyclical passage in *Metachirus*. These strain differences, at least in so far as the host-vector cycles are concerned, are influenced by the nature of the host and possibly of the vector through which recent passages have occurred.

These marsupials, when they are infected, do not so readily or so consistently infect normal mosquitoes as do two species of marmosets which have been studied.

The results of these laboratory experiments suggest that *Metachirus nudicaudatus* and *Marmosa cinerea* can, under favourable circumstances, serve as vertebrate hosts in the maintenance of certain strains of jungle yellow fever, but before they are incriminated as natural hosts of the virus, supporting epidemiological evidence is required. In a rather comprehensive field study in a region where the disease is endemic in the forests, no information was obtained which implied that marsupials played a significant rôle in the propagation of the virus [see this *Bulletin*, 1947, v. 44, 414].

F. O. MacCallum

HUGHES, T. P. & PERLOWAGORA, Alina. **The Reaction of certain Species of Bats to Yellow Fever Virus.** *Amer. J. Trop. Med.* 1948, Jan., v. 28, No. 1, 101–5.

The possibility that yellow fever virus may be disseminated between isolated forest patches through transport by flying vertebrates has been suggested frequently, but has been subjected to little experimental test. KUMM [see this *Bulletin*, 1933, v. 30, 6] failed to find virus in the blood stream of bats bitten by

Aëdes aegypti infected with either of two strains of yellow fever virus. More recently, LAEMMERT *et al.* [see this *Bulletin*, 1947, v. 44, 414] found that only one of 81 bat sera from an area of endemic yellow fever infection neutralized the virus, and they considered this one result non-specific.

Hughes and Perlowagora carried out a total of 254 tests for the presence of virus in the sera of bats which had been exposed to it, either by injection or by mosquito bite, but no virus was detected. Neither did any of the 55 bats which were tested develop neutralizing antibodies as a result of this exposure. They used *Eumops californicus*, *Phyllostomus panamensis* and *Molossus* sp. which frequent forest areas.

These results indicate that tests on sera of captured wild bats can give no information as to whether these vertebrates have previously been in contact with yellow fever virus. *F. O. MacCallum*

FOX, J. P., DA CUNHA, J. F. & KOSSOBUDZKI, S. L. **Additional Observations on the Duration of Humoral Immunity following Vaccination with the 17D Strain of Yellow Fever Virus.** *Amer. J. Hyg.* 1948, Jan., v. 47, No. 1, 64–70.

This is a report of examination of sera of several vaccinated groups in whom immunity has been followed for several years.

Though there has been some diminution in the percentage of individuals with strong protection in the mouse protection test, 4 to 6 years after inoculation practically all sera still contained detectable antibody. As in a previous study by FOX & CABRAL [this *Bulletin*, 1943, v. 40, 451], there was a suggestion of short duration of immunity in children, but the difference between results in children and older persons was not statistically significant.

These results, together with those of SMITHBURN and MAHAFFY in Uganda [see this *Bulletin*, 1946, v. 43, 34] and BUGHER and GAST-GALVIS in Colombia [*ibid.*, 1944, v. 41, 478] give complete support for the four-year certificate of immunity to yellow fever which is in current use. *F. O. MacCallum*

FROES, H. P. Proyecto de campaña continental para la erradicación del *Aëdes aegypti*. [**Scheme for a Pan-American Campaign towards the Eradication of** *Aëdes aegypti*.] *Bol. Oficina Sanitaria Panamericana.* 1947, Oct., v. 26, No. 10, 842–51. English summary.

See also p. 485, GIGLIOLI, **An Investigation of the House-frequenting Habits of Mosquitoes of the British Guiana Coastland in relation to the Use of DDT.**

DE CAIRES, P. F. *Aedes aegypti* **Control in the absence of a Piped Potable Water Supply.** *Amer. J. Trop. Med.* 1947, Nov., v. 27, No. 6, 733–43, 12 figs.

The classical *Aëdes aegypti* control measures, as established in Brazil by the International Health Division of the Rockefeller Foundation, were employed in British Guiana during the recent war years, the Colony having a vitally important source of supply of bauxite. Briefly, these measures amounted to a system of careful inspection of waters for larvae of *Aëdes aegypti*; this involved the provision of staff for inspection of water containers in and around dwellings, in dock-areas and shipping, and of water collections difficult of access; lastly other persons were trained for adult mosquito catching. *Aëdes aegypti* house indices (the percentage of houses inspected in which adult mosquitoes or water receptacles containing pupae, larvae or eggs were found) became low, but fluctuated with rainfall, and eradication was not achieved in urban areas. Persistence of breeding was contributed to by a 4-day egg-to-adult cycle which occurred at times; it was not practical nor economical to increase the inspection rate from a 7-day to a 4-day interval.

Georgetown (6° N 58° W) with a population of 90,000, has no piped potable water supply, and in consequence rainwater is collected from the roofs by galvanized roof gutters and the water is led into large storage containers such as vats, tanks, barrels and drums. The variety of breeding places, and the methods of inspection and control, are adequately described and illustrated. The necessity for strict discipline of inspection squads is stressed ; the process of constant checking of the work of inspectors, of discovering their inefficiencies, and bringing them to book, is unpleasant but essential.

The human factor of inefficiency in inspection is eliminated by the introduction of DDT applied on one occasion as a residual insecticide to the interior walls of all houses ; hidden foci of breeding are no longer a source of trouble. A five per cent. solution of DDT in kerosene is applied at an estimated dosage of 100 mgm. DDT per square foot of wall and ceiling. The cost for a 3 to 5-roomed house is about 1·76 dollars, which represents 0·47 to 0·59 dollars (British West Indies) per head of population. The overall cost is much cheaper than the cost of the classical inspection service ; in rural areas, the classical method could produce a zero index in four months at a cost of 1·39 dollars per head of population, urban costs being infinitely greater.

The Georgetown *Aëdes aegypti* house index, which under classical control methods fluctuated between 1 and 3 per cent., fell to zero within 12 months of the introduction of the use of DDT as a residual insecticide. In the event of *Aëdes* re-establishing breeding in an area, it is believed that a single localized re-application of DDT will be effective in eradicating the focus within a few weeks.

R. Ford Tredre

DENGUE AND ALLIED FEVERS

FLORIO, L. & MILLER, Mabel S. **Epidemiology of Colorado Tick Fever.** *Amer. J. Pub. Health.* 1948, Feb., v. 38, No. 2, 211–13.

The presence of the virus of Colorado tick fever was demonstrated by hamster inoculation in nine out of ten pools of ticks (*Dermacentor andersoni*) collected from areas in Denver where the disease is endemic.

In a study of experimental infection among ticks it was found that hamsters could be infected by the bites of larvae whose parents had been infected by biting infected hamsters. By inoculation experiments it was shown that larvae, nymphs, and adults belonging to the same brood of infected ticks were infective to hamsters, though the eggs of these broods were not infective.

Larval ticks fed on infected hamsters remained infective after reaching the nymphal and adult stages.

Dog ticks (*Dermacentor variabilis*) collected in Long Island, where the disease is not known to occur, were found to be infected with a virus similar to, or identical with, the virus of Colorado tick fever. *John W. D. Megaw*

PLAGUE

TIEH, T. H., LANDAUER, E., MIYAGAWA, F., KOBAYASHI, G. & OKAYASU, G. **Primary Pneumonic Plague in Mukden, 1946, and Report of 39 Cases with 3 Recoveries.** *J. Infect. Dis.* 1948, Jan.–Feb., v. 82, No. 1, 52–8, 3 figs. [20 refs.]

Primary pneumonic plague in Manchuria is not a new occurrence, for there were the epidemics of 1910 and 1920. What is new for this very fatal and

infective type of plague is the report of three recoveries. Although these cases occurred towards the end of the epidemic the circumstances point to the use of sulphadiazine as " the principal factor in the recovery " of three out of five patients treated. The authors believe that the infection was started by a carrier who came into Mukden during the incubation period and died after a very short illness. Contacts of proven cases of primary plague were quarantined: they numbered 67, and 23 of these developed plague. An interesting point is emphasized that, out of 42 individuals without symptoms, who had throat swabbings made daily, 4 were found to harbour virulent *P. pestis* and that this infection persisted for 6 to 15 days. " At least one of the 4 is believed to have been a true healthy carrier ". *W. F. Harvey*

PUBLIC HEALTH REP. Wash. 1948, Feb. 20, v. 63, No. 8, 243. **Plague Infection in Dawson County, Texas.**

As a result of evidence of plague in native rodents in Cochran County and in Dawson County, Texas in 1946 and 1947, respectively, the Texas State Dept. of Health, in co-operation with the U.S. Public Health Service, surveyed the ecology of the reservoirs and vectors of plague in the affected counties.

At the end of 1947 it was reported, as a result of these studies, that plague infection had been found again in Dawson County, eight miles west of Lamesa. The infection was detected in a pool of 141 fleas from 14 pack rats (*Neotoma micropus*). *H. J. O'D. Burke-Gaffney*

ARAUJO COSTA, Gobert. Contribuiçao ao diagnóstico da peste nos ratos. [**Diagnosis of Plague in Rats.**] *Monografias do Serviço Nacional de Peste. I.* Rio de Janeiro, Brasíl. 250 pp. [Bibliography.]

A monograph of 250 pages restricted to the diagnosis of plague in rats might be doubtfully regarded as a real work of reference. It may be stated, therefore, at the outset that the abundant information contained in it, after a full historical introduction of 50 pages, relates as much to bacteriology as to zoology. A full summary indicates how much is the author's own personal experience from the examination of 10,000 rats, by which only two were found to be infected with plague, in Rio de Janeiro, and how much is a penetrating analysis and test of claims made by other authors. A short set of conclusions is, itself, a summary, and the bibliography extends to 334 references, each of which is presented under full explanatory title. There are no illustrations and no graphs, but there are many full tables which are in many respects more useful than graphic presentations. We have now for some time been accustomed to very thorough deliverances on plague from America and owe a great deal of our knowledge of epizootic and enzootic plague to these. One might even, protestingly and without seriousness, speak of America as the " home " of plague, a mere counterblast to the description of India as the " home " of cholera. The fact that this work is written in Portuguese should not be a deterrent to its use by anyone who is well versed in the subject matter, for it is easy to read and is packed with information.

Some of the facts, or, as the case may be, conclusions, can be shortly set out :— The rats reached the laboratory in a varied condition, some 1,500 still alive, some recently dead and many in an advanced state of decomposition. Necropsies were undertaken in those of the species *R. norvegicus*, *R. r. alexandrinus*, *R. r. rattus* and *M. musculus*. Fleas on these rodents belonged in greatest number, 593 out of 598, to the species *X. brasiliensis* and *X. cheopis*. Special attention was paid to the possibility of organismal non-plague infections, contaminating and epizootic, which can lead the field worker astray in the

diagnosis of plague. Even *Trypanosoma lewisi* came in for attention, as might diseases like tularaemia and melioidosis. Contaminating organisms of coli-aerogenes, *Proteus* and *Salmonella* groups often give trouble morphologically. It is evident that the author separates the pasteurellas of the animal haemorrhagic septicaemias, which seem to be one for every animal (*ovis, bovis, suis, canis, caprae, cuniculi, gallinae* etc.) from *Pasteurella pestis*. The chief differentiation, however, that is obligatory in the rat is that of *P. pestis* from *P. pseudotuberculosis rodentium* and this receives full consideration.

Four methods are singled out for a presumptive test and these are designated, the classical method, the method of thermoprecipitation, that of bone marrow puncture and the flea examination. Full identification is supplementary to the presumptive test. The author maintains strongly the value of bone marrow examination in decomposed animals. A great many suggested culture media have been examined for their selective differentiation value and the characters of the plague bacillus which are stressed are: morphology; motility at 22°C. (Levinthal's method); fermentation of glucose, lactose and saccharose; the indole, methyl red and reductase tests and finally an inoculation, that is to say guineapig, test. Much valuable direction is given to the type of plague, acute and chronic, especially in the declining epizootic which may justly bear such names as mitigated, benign, resolving, residual and inapparent plague.

An index would add greatly to the value of this monograph as a reference work.

[It is rather surprising that in a great many extensive bibliographies, as this one is, there should be no reference to the Royal Indian Commission (1898–99) although we find references to German, Austrian, English and even Astrakan Commissions. In historical texts and in text books, too, the "Existence of an Endemic Focus of Plague in the Foothills of the Himalayas" is very little noticed although it was given a chapter in the Commission Report referred to, and by HANKIN (*Ann. Inst. Pasteur*, 1898, v. 12, 711). It existed before the arrival of plague at Bombay from Hong Kong and was said to be commonly preceded by a rat epizootic. Another constant omission, which is understandable considering the local character of the publications, is reference to the basic investigations of Glen Liston on rat-flea transmission of plague, and to Ashburton Thomson's Report on the Second Outbreak of Plague in Sydney, 1902. They formed very important supplements to the work of Simond in Bombay and were milestones on our path of knowledge. Liston's first study of "Plague, Rats and Fleas" and the part the latter played in the transfer of plague from rats to man was communicated to the Bombay Medical and Physical Society in February 1903, and a second to the Bombay Natural History Society in April 1903.] *W. F. Harvey*

CHOLERA

SMITH, W. E. & PENNELL, R. B. **Reducing the Pyrogenicity of Concentrated Protein Solutions.** *J. Bacteriology*. 1947, Dec., v. 54, No. 6, 715–18.

"The pyrogenicity of concentrated protein solutions can often be reduced by treatment with 'decalso', and by filtration through S-6 pads of the Republic series.

"The amount of 'decalso', and the area of pad space used are functions of the degree of pyrogenicity and of the protein concentration of the solution, and for maximum effectiveness they should be determined for each solution to be

examined. In practice, for 6 to 8 per cent. protein solutions of mild pyrogenicity, 30 g. of 'decalso' and 40 sq. inches of pad surface per liter of solution have given adequate reduction of pyrogenicity."

PASRICHA, C. L., PAUL, B. M., DAS GUPTA, A. C. & DAS, A. K. **Sulphadiazine in the Treatment of Cholera.** *Indian Med. Gaz.* 1947, Sept., v. 82, No. 9, 518.

"A series of 425 cholera patients were treated with sulphadiazine in addition to the usual saline supportive treatment. The death rate in this series was 8·2 per cent. A parallel series of 423 control cases not treated with sulphadiazine gave a death rate of 9·5 per cent.

"Another series of 451 cases treated with sulphadiazine was compared with a parallel series of 463 cases treated with sulphaguanidine. The mortality in the sulphadiazine series was 7·9 per cent. whereas in the sulphaguanidine series it was 4·3 per cent.

"Sulphadiazine in the dosage used had no beneficial effect on cholera."

PASRICHA, C. L., PAUL, B. M., DAS GUPTA, A. C. & DAS, A. K. **Sulphaguanidine in the Treatment of Cholera.** *Indian Med. Gaz* 1947, Sept., v. 82, No. 9, 518–20.

"A series of 1,118 hospitalized cholera patients were treated with sulphaguanidine with a death rate of 3·7 per cent. A parallel series of 1,170 control cases were treated in exactly the same way but not given sulphaguanidine and the death rate was 7·5 per cent. A series of 60 cholera patients were treated with sulphaguanidine in village homes. No supportive treatment was possible. The death rate in this series was 18·3 per cent., whereas in a parallel control series of 59 cases, the death rate was 40·7 per cent.

"Sulphaguanidine is thus of considerable value in the treatment of cholera."

SEAL, S. C. **Sulphaguanidine in the Treatment of Cholera under Rural Conditions. (A Report on 290 Cases).** *J. Indian Med. Ass.* 1947, Dec., v. 17, No. 3, 85–90.

Many reports now bear witness to the value of sulphaguanidine in the treatment of cholera in hospital patients. Such patients are generally late arrivals and the treatment might be more effective still at an earlier stage of the disease. The present account relates to 30 small outbreaks of cholera in 29 villages, where the treatment was carried out under actual field conditions in which both the community and the environment remained uncontrolled. The total number of cases was 290, and sulphaguanidine was used in 134, with only two deaths: the remainder, not alternate cases, but treated otherwise, furnished 67 deaths. The difference in the fatality rates is very significant, in the proportion of 1·5 to 43·5 per cent., respectively. No toxic symptoms could be ascribed to the sulphaguanidine, which was administered as initial dose of 3 gm. followed by further doses of 3 gm. every 3 hours, until stools were reduced in number to two or less per day, after which the dose became one gramme every 6 hours for the next 24 hours. The author considers that the drug may be safely kept in villages and administered generally in suspicious gastro-intestinal diseases "as an emergency or first aid measure."

W. F. Harvey

FLORESTANO, H. J. & BAHLER, M. E. **Investigation of some Newer Sulfonamides as Intestinal Chemotherapeutic Agents.** *J. Pharm. & Exper. Therap.* 1948, Feb., v. 92, No. 2, 196–206, 1 fig. [23 refs.]

"Preliminary study of three new sulfonamides as intestinal chemotherapeutic agents is reported: 2-sulfanilamido-5-carbamylthiazole, 2-(N^4-succinamylsulfanilamido)-thiazole, and 2-(N^4-succinylsulfanilamido)-1,3,4-thiadiazole.

"The presence of the carbamyl group in the 5-position of sulfathiazole greatly reduces absorption from the gastro-intestinal tract and activity in vitro. However, marked anti-coli action was demonstrated in mice and dogs. Sulfacarbamylthiazole is relatively stable and activity is apparently due to the drug per se.

"Replacement of the carboxy group of succinylsulfathiazole with the carbamyl group yields a compound considerably more labile than the parent drug. While absorption was slight following oral administration of succinamylsulfathiazole to mice and dogs, the drug showed but little anti-coli activity in vivo.

"Substitution of the succinyl radical in the N^4-position of sulfathiadiazole results in a compound highly active in the intestinal tract of both mice and dogs and only slightly absorbed into the blood. The anti-coli activity of succinylsulfathiadiazole was found to be much greater than that of sulfathalidine in mice and about equal to the latter drug in dogs. Data seem to establish succinylsulfathiadiazole as a potentially useful drug for trial in therapy of enteric infections."

BHATNAGAR, S. S., FERNANDES, F., DE SA, J. & DIVEKAR, P. V. **A New Sulpha Compound ("6257") and its Use in Human Cholera Infection.** [Correspondence.] *Nature.* 1948, Mar. 13, 395–6.

Sulphonamides have become currently used drugs in cholera. A new compound is now put forward with considerable promise of cure. It is described as "a condensation product of two molecules of 2 p-amino-benzene sulphonamido-thiazole ('Cibazol') and three molecules of formaldehyde" with molar weight much greater than that of any other sulpha compound so far employed in clinical therapy.

In vitro experiments have shown this substance to have bacteriostatic power and, in greater concentration, powerful bactericidal action. Further experimentation *in vivo* on mice gave indication that pre-infectional administration by subcutaneous or intraperitoneal routes could protect mice against intraperitoneal injection of 2 MLD of cholera vibrios. The drug has already been tried in the field in total dosage of 28 gm. "given as 10 gm. on the first day, two doses of 4 gm. on the second day and two 1 gm. each morning and evening every subsequent day for five days." Some 85 cases of bacteriologically established cholera have undergone treatment and the mortality was only 4 per cent. presenting a marked contrast to the estimated mortality of "more than 60 per cent. during the past seven years." It is important to note that no toxic effects, even with a maximum dose of 50 gm., were observed. The drug may also be used prophylactically. *W. F. Harvey*

AMOEBIASIS AND INTESTINAL PROTOZOAL INFECTIONS

STARKEY, H. & POOLE, J. **Survey of Intestinal Parasites in Repatriated Prisoners of War from Hong Kong.** *Canadian Med. Ass. J.* 1947, Oct., v. 57, No. 4, 377–9.

The authors examined the stools of 453 Canadian ex-prisoners of war from Hong Kong several months after their repatriation to Quebec and the Maritime Provinces. Normal stools were examined daily for 3 days and again on the 5th and 6th days: on the 4th day a fresh specimen was examined after purgation. Direct examination for parasites was made in saline and identification was based on stained preparation: washed stools were examined for cysts by the standard zinc sulphate flotation method.

In 231 cases parasites were found in normal stools and in 41 they were only found after purgation. In many cases they were found in the specimens of the 5th and 6th days and not in the purge specimen itself.

Pathogenic parasites were found in 26·7 per cent. of cases and non-pathogenic in 41·3 per cent. Of the former, *Giardia* and *Ascaris* accounted for some 9 per cent. each, *E. histolytica* for 7 per cent. and *Ancylostoma* for 4 per cent. (It is pointed out that these percentages are individual, owing to the presence of mixed infections in some cases.)

E. coli was found in 36·4 per cent., *Endolimax nana* in 22·5 and *Trichuris trichiura* in 17 per cent.

Other parasites were found in less than 3 per cent. of patients.

The findings are analysed in relation to a history of amoebic dysentery, of intestinal upsets, of general asthenia and of no complaints since return to Canada.

From this analysis, it is revealed that *E. histolytica* occurred in 3·6 per cent. of those without histories or symptoms of acute amoebic dysentery since returning to Canada; in 7·5 per cent. of those with a definite history; and in 9·5 per cent. of those with vague symptoms.

It is pointed out that the group under survey had been examined, and where necessary treated, on their arrival in Canada.

The authors refer to the findings of MILLER (*Canadian Med. Ass. J.* 1946, v. 55, 336) who suggested that the incidence of *E. histolytica* in the general population of Canada was probably about 2 per cent.: in the present survey it was about 7 per cent. The only sub-group in this survey approximating to the incidence quoted for the general population was that of men having no history of typical amoebic dysentery and no complaints since returning to Canada (3·6 per cent.).

The authors conclude that in routine survey of faeces for parasites, it is desirable to include a purge in the routine, and also to examine more specimens for at least two days thereafter. They also conclude that those who were prisoners of war in the Far East carry a higher percentage of pathogenic intestinal parasites than do residents of Canada.

H. J. O'D. Burke-Gaffney

ANDERSON, H. H. & HANSEN, E. L. **Cultivation of** *Endameba histolytica*. *Liber Jubilaris J. Rodhain* (*Soc. Belge Méd. Trop., Brussels*). 1947, Dec., 47–61, 2 figs. [43 refs.]

The authors trace the development of media for the cultivation of *E. histolytica* since BOECK and DRBHOLAV's success in 1925. They finally describe a new medium containing only synthetic products. There are 12 amino-acids nucleic acid, rice powder, cholesterol, 11 vitamins and various salts. In it, with only a single bacillus "t", over 170 compounds have been tested for their

amoebicidal activity. Contrary to expectation, based on LAIDLAW's findings with emetine, various agents were not uniformly more active in the liquid medium. The activity of the arsenoxides was lower in the liquid medium than in that with a solid base. With most other chemical types only insignificant differences were noted. It is hoped that a medium containing only synthetic ingredients may afford an understanding of the growth requirements of *E. histolytica*. *C. M. Wenyon*

DOBELL, C. **An Improved Method for testing the Action of Emetine and other Chemicals on *Entamoeba histolytica* in Cultures.** *Liber Jubilaris J. Rodhain* (*Soc. Belge Méd. Trop., Brussels*). 1947, Dec., 201–11. [15 refs.]

By the use of a liquid medium consisting of dilute horse-serum (1 : 8 Ringer's fluid) with rice starch and 0·2 per cent. disodium hydrogen phosphate as buffer, cultures of *E. histolytica* have been obtained and used for testing the action of emetine. This medium, first described by LAIDLAW, DOBELL and BISHOP in 1928, has been employed by Dobell since then. The amoebic culture has been purified so that *E. histolytica* with the single organism *Bact. coli* have been obtained. In order to ensure that the amoebae grow in subculture, the medium is inoculated with the bacillus and incubated for 24 hours before the amoebic subculture is made into it. In this way it has been shown that emetine in a strength of 1 : 5,000,000 is invariably fatal to *E. histolytica* within 4 days and that they sometimes succumb to dilutions of 1 : 20,000,000. The author thinks that by following the technique described in the paper there is an opportunity of testing the action of other substances which are calculated to cure amoebic dysentery. *C. M. Wenyon*

SIGUIER, F., SARRAZIN, A. & PÉRIER, R. Typhlo-hépatite amibienne récidivante à court terme évoluant depuis deux ans chez une coloniale transplantée. [**Amoebic Typhlo-Hepatitis with Frequent Relapses at Short Intervals during Two Years.**] *Bull. et Mém. Soc. Méd. Hôpit. de Paris.* 1948, Nos. 1/2, 27–30.

The authors describe a condition they refer to as an amoebic typhlo-hepatitis with frequent relapses at short intervals. The symptoms and signs are inconclusive, but there is infiltration of the caeco-colic region in association with hepatic pain and discomfort; and prostration. This liver trouble recurs at short intervals ; in some cases it resolves spontaneously, in others it responds to emetine, and in yet others it is resistant to emetine.

They describe in detail such a case of suspected liver involvement without any evidence of frank abscess ; this was treated for over two years on each recurrence with emetine with temporary benefit. The patient in due course showed evidence of emetine poisoning ; and she finally absconded. *A. R. D. Adams*

KULLMAN, H. J. F. & GOLDEN, H. **Hepatic Amebiasis.** *U.S. Nav. Med. Bull.* 1948, Jan.–Feb., v. 48, No. 1, 22–39, 10 figs. [14 refs.]

In the sense of this paper, the term hepatic amoebiasis covers amoebic hepatitis and amoebic abscess of the liver. The three possible routes of invasion by the amoeba are discussed : (1) Direct extension through the bowel wall, peritoneal cavity and capsule of the liver ; (2) Extension by the lymphatic route ; (3) Extension from the bowel through tributaries of the portal vein, generally considered to be the most common method.

Hepatic amoebiasis is suggested in cases which fail to respond to penicillin therapy with or without sulphonamide, and which present signs pointing to

acute liver disease, with or without jaundice, and accompanied by leucocytosis, chills and fever. The elimination of intestinal amoebic infection forms an important part in the treatment of hepatic amoebiasis. In the six cases detailed in this report, open operation and aspiration were avoided. This is ascribed to early recognition and intensive treatment with emetine injections and diodoquin : where secondary infection is present (and it is suggested that 50 per cent. of amoebic abscesses of the liver are so infected at the time of diagnosis) penicillin and emetine would appear to be a wise combination. One case with constant lumbar pain is described which suggested formation of an amoebic perinephric abscess. The pain and fever were relieved by emetine injections. The method of pneumoperitoneum is employed as a means of delimitating the lower edge of the liver. Penicillin therapy alone is regarded as of no value, but should be considered a valuable adjunct to emetine when secondary invading organisms are suspected. *P. Manson-Bahr*

HAYS, T. G., BROWN, R. B. & GODFREY, E. W. **Liver Abscess.** *U.S. Nav. Med. Bull.* 1948, Jan.–Feb., v. 48, No. 1, 7–21, 5 figs.

During five months from December 1945 to May 1946, 10 cases of liver abscess were treated in a U.S. Naval Hospital. Several of them illustrate many important points in diagnosis and treatment. The clinical picture may be anything but characteristic. The pain in the right lobe of the liver is usually dull and intensified by deep pressure.

Laboratory studies may be of limited diagnostic value, and liver function tests, even the icterus index, and the van den Bergh reaction, are not uniformly or significantly altered. The most reliable aid to diagnosis is provided by radiography. Elevation of the right dome of the diaphragm is purely mechanical; restriction of movement is primarily irritative and increases with proximity of the abscess to the dome. Areas of atelectasis or pneumonitis within the lung tissue, or fluid in the pleural sulcus, are secondary to the inflammatory process below the diaphragm. Serial films, showing increasing size of the liver, or progressive elevation of the dome of the diaphragm, are of particular significance.

The cases here recorded were treated by open surgical drainage, but it is admitted that some of the patients might have been cured on a more conservative régime. Seven of the ten cases were correctly diagnosed before operation. Two were operated as cases of acute cholecystitis and in one the true diagnosis was revealed post-mortem.

Three in whom amoebiasis was suspected as the chief aetiological factor returned with further complications attributable to this infection. Initial prompt, but incomplete, therapeutic response to penicillin on two occasions in one case, suggested a superimposed bacterial infection, though this was not confirmed at operation and by culture. It is suggested that more intensive treatment of the underlying amoebiasis with emetine and carbarsone might have prevented recurrences. *P. Manson-Bahr*

MANSON-BAHR, P. **Secondary Bacterial Infections of Amoebic Abscess of the Liver.** *Liber Jubilaris J. Rodhain* (*Soc. Belge Méd. Trop., Brussels*). 1947, Dec., 291–301, 5 figs. [13 refs.]

In the diagnosis and treatment of amoebic liver abscess, the possibility of secondary bacterial infection must always be considered. In abscesses of old standing, such contamination is not uncommon. The implications of its existence are insufficiently appreciated. Early cases of hepatic amoebiasis

respond well to emetine; later cases may fail to do so owing to bacillary infection, and repeated aspiration fails to relieve these. After surgical drainage such cases recover.

There is little reference in the literature of the last 35 years to proven secondary infection of amoebic liver abscesses, and none as to the route of infection when it does occur. In 60 of the author's cases of amoebic liver abscess, five were found to be bacterially infected; in only four of these could active amoebae be found in the aspirated abscess contents. *E. histolytica* cysts were recovered from the stools of 45 per cent. of patients with amoebic liver abscesses.

The author envisages the development of an amoebic liver abscess as follows: There is a massive portal invasion of the liver with amoebae, producing an allergic response with engorgement and swelling of the organ to about twice its normal size. Large numbers of amoebae are distributed throughout the liver lobules, but the majority are destroyed. A few survive and multiply at a focal point causing a single abscess, which initially resembles a gumma or a tuberculoma rather than an "abscess". In this solid slough the amoebae multiply at the periphery, and are not found in the centre. The centre of the lesion liquefies by cytolytic action; the liquefaction extends radially; and the contents of the cavity become a sterile fluid pus. In some rare cases this becomes inspissated, and absorbed or calcified. The author has seen four calcified abscesses, one of over 20 years' duration without the patient's having been aware of its presence. Aspiration of the pus before liquefaction takes place is impossible; but emetine injections kill the amoebae, and the material is absorbed. After liquefaction has taken place, emetine is not effective unless the pus is drained. If this pus is bacterially infected aspiration is inadequate, and emetine therapy is ineffective. Surgical drainage is necessary.

The routes by which bacterial infection of the liver parenchyma may occur are—(1) by rupture of the abscess through the diaphragm and direct infection via the respiratory tract; this is probably the most common; (2) by direct absorption from the large intestine, possibly by extension from the hepatic flexure of the colon in close proximity to the liver, by *Bact. coli* and other intestinal organisms; (3) as part of a general septicaemia from a septic focus such as a boil on the surface of the body.

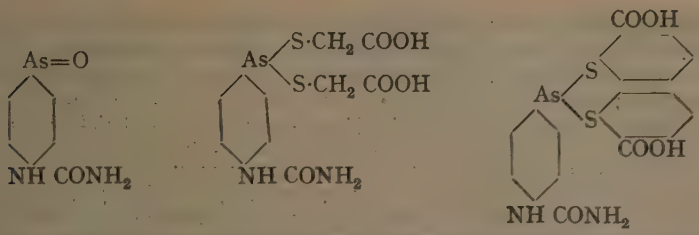
Five cases of amoebic liver abscess, secondarily invaded by bacteria, are cited to illustrate these modes of bacterial infection. The invading organisms identified were *Bact. coli* and a long-chain *Streptococcus*, *Strep. viridans*, *Salm. enteritidis*, and *Staphylococcus aureus*. In conclusion, the author contends that it is better to regard an amoebic liver abscess as bacterially infected until proven otherwise. Alteration in the temperature chart from an intermittent to a high remittent type is indicative of this secondary infection.

A. R. D. Adams

Cox, A. I. & Achuton. **A Case of Amoeboma with Abscess Formation followed by Infection of the Drainage Wound.** *Indian Med. Gaz.* 1947, Sept., v. 82, No. 9, 536–8.

Anderson, H. H., Hansen, E. L., Sah, P. P. T. & Cafiso, J. R. **Amebacidal and Pharmacologic Activities of Carbarsone Oxide (P-Carbamidophenylarsenous Oxide) and its Dithiocarboxymethyl and Dithiocarboxyphenyl Derivatives.** *J. Pharm. & Exper. Therap.* 1947, Oct., v. 91, No. 2, 112–23. [11 refs.]

Carbarsone has been used extensively in the treatment of amoebiasis. The corresponding carbarsone oxide and the dithio derivatives named in the title have the following formulae:—



The amoebicidal action of these four substances and of emetine have been compared *in vivo* and *in vitro* by the methods previously described by the authors [this *Bulletin* 1947, v. 44, 819]. Before clinical trials on monkeys naturally infected with *E. histolytica*, toxicity tests were carried out on the white cells of rabbits and on various laboratory animals. The pathological effects produced were studied in some detail. In the monkey, carbarsone oxide and the above derivatives were found more active than the pentavalent carbarsone, while emetine in effective doses was not well tolerated. Details are given of the methods employed in studying the distribution of arsenic in tissues after administration of arsenicals by different routes. Carbarsone oxide gave rise to high levels of arsenic in bile, blood and urine, and smaller amounts were present in other tissues. The distribution of arsenic after dithio derivatives was somewhat different and levels were not so high. The level remained appreciable for some days after administration. The amount bound by tissues was roughly parallelled by toxicity. Fewer pathological changes were produced by the dithio derivatives than by the parent oxide. The introduction of these groupings did not, however, appreciably affect amoebicidal activity *in vitro* or *in vivo*. *J. D. Fulton*

Goodwin, L. G., Hoare, C. A. & Sharp, T. M. **The Chemotherapy of Amoebiasis. Part I. Introduction and Methods of Biological Assay.** *Brit. J. Pharmacol.* 1948, Mar., v. 3, No. 1, 44–8. [22 refs.]

Goodson, J. A., Goodwin, L. G., Gorvin, J. H., Goss, M. D., Kirby, K. S., Lock, J. A., Neal, R. A., Sharp, T. M. & Solomon, W. **The Chemotherapy of Amoebiasis. Part II. Amines derived formally from Emetine.** *Ibid.* 49–61.

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I. In this series of papers is described a systematic search for new amoebicides whose structure has been based on that of emetine and of certain compounds found by Pyman (*Rep. Brit. Ass.* 1937, v. 107, 60) to be active *in vitro*. Methods for comparing the activity of these substances *in vitro* and *in vivo* are described. For the former tests, a culture of *E. histolytica* grown with a single bacterium (*Bact. coli*) was maintained in culture on the horse-serum-Ringer-egg medium of Dobell & Laidlaw [this *Bulletin*, 1927, v. 24, 363]. In the actual test the buffered horse-serum Ringer medium of Laidlaw *et al.* [this *Bulletin*, 1929, v. 26, 469] was used to which the appropriate concentration of drug in sterile buffered Ringer solution was added and then a heavy inoculum of *Bact. coli* and a small quantity of sterile rice starch. After incubation at 37°C. overnight, the bleaching of an added drop of dilute methylene blue solution indicated that conditions in the medium were satisfactory for the growth of amoebae. A heavy suspension of *E. histolytica* from the stock cultures was then added to each tube by pipette. After incubation for 3 days, the contents of the tubes were

examined microscopically for the growth of amoebae, the *p*H of the solution was checked and the viability of the bacteria tested by subculture. The *in vivo* tests in which young rats of weight 20 to 30 gm. were used immediately after weaning were carried out in a manner similar to that described by JONES [this *Bulletin*, 1947, v. 44, 313] by intracaecal inoculation of 0.2 to 0·4 cc. of *E. histolytica* culture material. The present authors point out that while numerous shallow ulcers were produced in these rats which have a restricted parasite population on account of their age, nothing resembling the deep flask-shaped ulcers seen in human infections was encountered. The inoculated amoebae were found to have ingested bacteria, but rarely red cells, and cysts were scanty. Natural infections of the experimental rats with an amoebae, not distinguishable in fresh preparations from *E. histolytica*, caused difficulty. It was believed that infection arose from cysts passed by hamsters housed in the same room. With suitable precautions, infection of the rats could be avoided. [FULTON & JOYNER had difficulty with similar infections in rats while carrying out amoebicidal tests and have recently reported (this *Bulletin*, 1948, v. 45, 430) the results of a survey of amoebic infections in laboratory rodents—white rats, cotton rats, hamsters and Orkney voles separately housed were found to be infected very early in life, about 50 per cent. in the case of white rats before weaning. The cotton rats had been isolated since coming to Britain.] Differences in infectivity of human strains of *E. histolytica* for these young rats were noted and the infection rate in different experiments varied from 80 to 100 per cent. Drugs were generally administered in the diet for 6 days, but if it were rendered unpalatable in a promising case, drug dosage by stomach tube was resorted to. The criterion of activity of a drug was the presence or absence of amoebae in the rat caeca after treatment ; the macroscopic appearance of that organ was also taken into consideration. Controls were used in all experiments. The results for a series of standard amoebicides tested by both methods is given in tabular form. Emetine proved the most active drug in both cases (based on dosage given), and the relative activity of the others was in the same sequence in both tests, but this was not true for all drugs. The calculation of chemotherapeutic indices showed that the curative dose of emetine was close to the toxic dose. Diodoquin had the best therapeutic index.

II. A number of compounds based on structures derivable from emetine were previously synthesized by PYMAN and collaborators but proved inactive against *E. histolytica in vitro*. The present authors have prepared and tested two series of secondary diamines of the general type Ph.R.NH.R.NH.R.Ph (phenylalkylamine series) formally related to emetine, in which Ph represents a benzene ring, R a chain of CH_2 groups. This change was varied in length and structure and different substituent groups were introduced to the benzene ring. In a second alkylamine series, the phenyl groups were omitted. The test methods were similar to those employed in Part I above. The results are given in very condensed form in a table and include those for tests carried out on certain trypanosomal, leishmanial and malarial infections. There is also a chemical section and in order to appreciate the effort involved in these researches the original should be consulted. Certain derivatives in the phenylalkylamine series showed activity both *in vitro* and *in vivo* and the authors discuss the effect of different substituents as well as of variations in length of the methylene chain. Broadly speaking, the results for the alkylamine series were similar. The difference in activity between soluble and insoluble salts of the bases, including bismuth iodides, was not significant. None of the compounds was so active as emetine, many were irritant and it appeared that clinical trials were not justified.

III. PYMAN (*Rep. Brit. Ass.* 1937, v. 107, 57) reported that 1 : 10-bis (di-*n*-amylamino) decane $(C_5H_{11})_2N(CH_2)_{10}N(C_5H_{11})_2$ showed high amoebicidal

activity *in vitro*. Following this observation, the present authors have synthesized a number of compounds, including aromatic derivatives, based on the model of the above substance and have studied the effect on amoebicidal activity of changes in its structure as well as in those of the corresponding secondary bases and certain quaternary ammonium salts. The tests are presented as in Part II above and a chemical section is included. The parent substance showed activity *in vitro* but only to a slight extent *in vivo*. Tertiary aromatic diamines of varied structure were inactive in both tests, while the corresponding secondary aromatic diamines showed slight activity *in vitro*. Secondary araliphatic amines were active to some extent *in vitro*, but not *in vivo*, and results with this series indicated that an *in vitro* test by itself is unreliable for assessment of amoebicidal action. As shown in Part I above the two types of test give inconsistent results in the case of diodoquin (a very insoluble substance). Quaternary ammonium salts proved a little more active than the parent tertiary bases.

J. D. Fulton

MILLER, A. A. & PECK, C. R. **Balantidial Dysentery. Report of a Fatal Case in Assam.** *Brit. Med. J.* 1948, Mar. 6, 448–9, 1 fig. on pl.

The authors report this case because of the rarity of balantidial dysentery, especially in India: but they refer in a footnote to 10 cases, reported by SHUN-SHIN [this *Bulletin*, 1948, v. 45, 84] in the island of Rodriguez, since their article was completed.

The present case refers to an Indian sepoy of 30 who died of an acute dysenteric illness three days after admission to hospital, and five days after symptoms began. The principal clinical features were pyrexia, abdominal pain, diarrhoea and dehydration. No pathogenic organisms could be found on repeated microscopical and cultural examination, but a number of parasites were found in an ulcerated portion of the pelvic colon: the disposition and morphology of these organisms are fully described, together with the histopathology of the ulcerated colon. These parasites had the typical morphology of *Balantidium coli*. The authors point out that although the clinical, autopsy and histological features of this case were similar to those often found in amoebic dysentery, the discovery of the balantidia suggested an alternative diagnosis.

H. J. O'D. Burke-Gaffney

KIRSHBAUM, J. D. **Intestinal Coccidiosis. Report of Two Cases of** *Isospora hominis*. *Amer. J. Clin. Path.* 1948, Jan., v. 18, No. 1, 58–60, 1 fig.

"During the course of examining approximately 5,000 stool specimens for parasites, in a general hospital at Espiritu Santo in the New Hebrides, two infections with *Isospora hominis* were encountered. Both soldiers were members of the same company, both manifested mild intestinal symptoms of intermittent diarrhea, malaise and loss of weight, and both responded promptly to treatment. Eosinophilia was present in both patients. The oocysts and sporocysts were the only stages seen in both the fresh stool specimens and in specimens kept at room temperature for a period of sixty-six days. The cysts were easily identified in the fresh feces emulsified in water and also by the flotation method, using zinc sulfate or table salt."

RELAPSING FEVER AND OTHER SPIROCHAETOSES

WILLCOX, P. H. **Louse-borne Relapsing Fever in Persia.** [Correspondence.] *Brit. Med. J.* 1948, Mar. 6, 473.

The writer of this letter refers to the paper of BODMAN and STEWART [this *Bulletin*, 1948, v. 45, 433] in which the claim was made that louse-borne relapsing

fever had not been reported previously in Persia. He refers to a review of the subject in 1920 by WILLCOX (*Proc. Roy. Soc. Med.*, 1920, v. 13, Sect. of Med., 59) and LEDINGHAM (*ibid.*, 81) based on experiences in the 1914–18 war, during which the disease was a serious problem among British Forces in Iraq and Persia: both typhus and relapsing fever were endemic and were commoner than enteric fever.

Louse infestation was extremely common in the Turkish army and relapsing fever was prevalent in Kut in the winter of 1915–16: British troops did not become infected until their contact with the local population and with Turkish prisoners. It is also noted that the disease occurred in the civil and military population of Bagdad in 1917, and mortality figures are given for 1,883 cases.

It is also pointed out that Ledingham (*loc. cit*) had also demonstrated the correspondence in incidence curves for typhus and relapsing fever from 1917 onwards; and in other respects, epidemiological and clinical, the earlier epidemic of relapsing fever corresponded closely in almost every detail with the 1946 outbreak.

Evidence is quoted to show that lice may occasionally be infective for typhus and relapsing fever at the same time, and the case is mentioned of a medical officer who contracted relapsing fever 6 days after attending two cases of typhus.

H. J. O'D. Burke-Gaffney

BALLIF, L., CONSTANTINESCO, N. & CHELĂRESCO, M., Mme. Recherche des spirochétolysines dans la fièvre récurrente épidémique. (Note préliminaire). [**Lysis Test in Epidemic Relapsing Fever.**] *Bull. Acad. Méd. Roumanie.* 1946, v. 19, Nos. 4/6, 572–5.

The difficulty of diagnosing relapsing fever during the afebrile period when spirochaetes are absent from the blood led the authors to elaborate a lysis test. In this test, dilutions of the patient's serum (from 1/1 to 1/20,000) are mixed with defibrinated blood from a patient heavily infected with spirochaetes, and with guineapig or human complement. After incubation at 39°–41°C. for 2 hours, smear or thick drop films are prepared from each dilution, and are stained by Giemsa's method. The test is considered positive when the spirochaetes show numerous acidophile granules. The organisms may degenerate into indistinguishable masses of agglutinated granules or, with prolonged incubation of the mixtures, may be partially or completely lysed.

If dried blood only is available, it should be mixed with an equal volume of physiological saline and the extract used instead of serum.

The antibodies responsible for this reaction can be demonstrated at least 406 days after recovery from the disease and, as noted above, they can be recovered from dried blood. The test is therefore useful in epidemiological surveys or in field diagnosis in times of epidemics. [No evidence is offered that these lytic antibodies will react with the numerous and serologically distinct relapse strains of the spirochaetes. Without such proof, any information derived from the test could have little practical diagnostic value.]

J. C. Broom

PASTOR BOTIJA, F. Consideraciones sobre las secuelas oculares en la fiebre recurrente: epidemia de los años 1945–1946 en la Zona de Protectorado Español en Marruecos. [**Ocular Sequelae of Relapsing Fever, seen in the 1945–46 Outbreak in Spanish Morocco.**] *Med. Colonial.* Madrid. 1948, Feb. 1, v. 11, No. 2, 86–97.

The author states that though many have written on relapsing fever few have referred to the eye complications and sequelae of this disease. In the louse-borne outbreak of 1945–46, he observed certain cases which he wishes to

place on record and he refers in the present article to seven of them. The complications and sequelae mentioned are subconjunctival haemorrhage and purulent conjunctivitis, iritis and irido-cyclitis and uveitis, occasionally bilateral, more often unilateral and affecting nearly always the right eye. He also saw cases, one severe, of papillitis, with pallor of disk and some atrophy. The Wassermann reaction was not tried in all cases and may have been positive, but by no means in all. The conclusion is that the lesions were due to the relapsing fever and not to syphilis. The author is of opinion that if the infection were treated properly in the early stages with adequate doses of novarsenobenzol, these complications might be avoided. *H. Harold Scott*

DAVIS, G. E. **A Note on the Larval Stage of the Argasid Tick** *Ornithodoros moubata* **(Murray) 1877.** *J. Parasitology.* 1947, Dec., v. 33, No. 6, 495–6.

LEPROSY

DOULL, J. A., GUINTO, R. S., BANCROFT, Huldah & RODRIGUEZ, J. N. **Historical Inquiry as a Method of estimating the Trend of Leprosy.** *Internat. J. Leprosy.* Cleveland, Ohio. 1947, Oct.–Dec., v. 15, No. 4, 369–77.

The data used were collected in the municipalities of Cordova and Talisay in the province of Cebu, Philippine Islands, a detailed history being obtained for every household, including, to the utmost extent, all births, deaths, other entries and exits and the occurrence of leprosy. Sufficiently complete records were obtained for 3,204 families including 21,791 individuals, 335,016 person-years of exposure and 402 cases of leprosy (of which 261 were lepromatous and 141 neural or mixed). When the period of observation is divided broadly into years prior and years subsequent to January 1st, 1915, there is no evidence of any change in the total incidence rate. In the later years, however, the milder forms of macular and neural leprosy would have been more frequently observed than in the earlier period. Limiting the comparison to the lepromatous type reveals a lower rate post-1915. A more exact comparison is made by taking persons born between 1896 and 1910, and calculating their experience up to 1920, and comparing them with individuals born between 1911 and 1925, and calculating their experience up to 1935. After adjustments for age differences in the populations at risk, the resulting incidence rates of lepromatous leprosy per 1,000 person-years are: born in 1896–1910, followed to 1920, males 1·59, females 0·78, both sexes 1·18; born in 1911–25, followed to 1935, males 0·78, females 0·31, both sexes 0·54. The later born have rates only some half those of the earlier born. Further analysis of these two groups was made to show whether this downward trend occurred in leprous households as distinguished from the total population. Only those who were known to have been living in household association with lepromatous leprosy were considered as exposed and their experience was contrasted with that of those for whom no history of exposure to any type of leprosy could be ascertained. To make allowance for the incubation period, exposures only to 1915 for the first group and only to 1930 for the second were counted. The resulting rates, adjusted for age, and per 1,000 person years were as follows: Household exposure; earlier period, males 12·8, females 9·5, both sexes 11·3; later period, males 6·3, females 3·0, both sexes 4·7: no household exposure; earlier period, males 0·80, females 0·46, both sexes 0·63; later period, males 0·43, females 0·19, both sexes 0·32. The relative reduction is slightly greater in the leprous households.

Compulsory segregation was introduced in 1907 and the observed lower rates are in accord with the view that this may have been a factor. The experience is, however, relatively small and other environmental changes took place concurrently—in particular a rise in the standard of living—so this interpretation of the trend is not justified. *A. Bradford Hill*

SEN, P. **Need for a Study of Social Components in Leprosy.** *Internat. Med. Abstracts & Reviews.* Calcutta. 1947, Nov., v. 2, No. 5, 161–5.

HELMINTHIASIS

RAI, B. B. **Some Misleading Cases of Helminthic Infestation.** *Indian Med. Gaz.* 1947, Sept., v. 82, No. 9, 538–9.

VON BRAND, T. & FILES, Virginia S. **Chemical and Histological Observations on the Influence of** *Schistosoma mansoni* **Infection on** *Australorbis glabratus.* *J. Parasitology.* 1947, Dec., v. 33, No. 6, 476–82. [19 refs.]

"Infection with *Schistosoma mansoni* does not interfere seriously with the storage of fat in the body of its invertebrate host, the snail *Australorbis glabratus.* The latter's oxygen consumption also remains normal. Infected snails have, however, a reduced polysaccharide content and this reduction is a result of a diminished storage both in parasitized and non-parasitized organs. Whether this decrease is due to an impaired carbohydrate digestion and resorption, or to a toxic action by the parasites is not clear. The possibility that it is due to the food consumption of the parasites, has not been ruled out completely."

KIESER, J. A. **Schistosomiasis : an Educational Problem.** *South African Med. J.* 1947, Nov. 22, v. 21, No. 22, 854–5.

In this short paper the author stresses the deleterious effect of schistosomiasis [*S. haematobium*] on intelligence and vigour. "The mental symptoms are so monotonously uniform in character that a diagnosis of schistosomiasis could almost be made on them alone." In children they are "forgetfulness, indifference to punishment, apparent laziness and a disinclination to mental exertion combined with a sometimes very marked nervous irritability, obstreperousness and mental fatigue." This condition may be so serious that the child may be in danger of certification as mentally deficient.

Several illustrative cases are quoted, in children and young adults. Successful treatment removes these disabilities very effectively.

Charles Wilcocks

BLAIR, D. M., HAWKING, F. & ROSS, W. F. **The Effect of Miracil D on Human Schistosomiasis.** *Lancet.* 1947, Dec. 20, 911–12.

Miracil D is the hydrochloride of Miracil [see this *Bulletin*, 1948, v. 45, 96], and has been claimed by KIKUTH and GONNERT to be effective against infection with *Schistosoma mansoni* in mice and monkeys. The authors, after two of them had investigated its pharmacology and toxicology in monkeys and man, tried it on 42 patients in Southern Rhodesia, infected with *S. haematobium*, *S. mansoni* or both.

The drug was given by the mouth, as uncoated tablets, once each day after the midday meal, for 6 days each week, up to a maximum of 26 doses. Doses varied ; children were given 100–300 mgm. at a time, the three adults received doses of 200 mgm. Preliminary doses of 50 mgm. were given to all patients, to exclude idiosyncrasy. The drug was well tolerated, but these doses approach

the known maximum tolerated dose for repeated administration, namely 200–300 mgm. per diem.

Results were poor. Eight weeks after cessation of treatment only 9 of 40 with *S. haematobium*, and 2 of 11 with *S. mansoni*, were not passing eggs.

This is a preliminary paper, details are to be published elsewhere.

Charles Wilcocks

KHALIL, M. & HALAWANI, A. **Cloroben as Snail Poison for Control of Bilharziasis—its Danger to the Rice Plant.** *J. Roy. Egyptian Med. Ass.* 1947, Sept., v. 30, No. 9, 454–60.

Cloroben is an American preparation recommended for killing aquatic plants and snails. Analysis indicated that it contains 61·3 per cent. of ortho-dichlorobenzene as an emulsion. The authors found that 50 parts per million would kill *Bulinus truncatus* and *Planorbis boissyi* in 2–3 days, but that this concentration was lethal to fish (*Gambusia*) and to rice. Moreover, it is (no doubt) toxic for man and domestic animals. For these reasons the authors have issued a warning against the use of this substance in small control. Copper sulphate, which has been found to have a beneficial effect on rice fields by killing the algae which cause one of the important diseases of rice, remains the chemical of choice for this purpose.

Charles Wilcocks

LIPPINCOTT, S. W., ELLERBROOK, L. D., RHEES, M. & MASON, P. **A Study of the Distribution and Fate of Antimony when used as Tartar Emetic and Fuadin in the Treatment of American Soldiers with Schistosomiasis Japonica.** *J. Clin. Investigation.* 1947, May, v. 26, No. 3, 370–78, 5 figs.

American soldiers numbering 138, who had been infected with *Schistosoma japonicum* while serving in the Philippines and were still passing eggs in their faeces in spite of treatment, were given one or more courses of tartar emetic or Fouadin, equivalent to 45 mgm. Sb on alternate days. The latter was given intramuscularly and tartar emetic was given intravenously till a total of approximately 570 mgm. of Sb was reached. Estimations of Sb in body fluids, as well as of the amount and rate of excretion in urine and faeces, were made on some patients during and after treatment by the Rhodamine B method of MAREN (*Bull. Johns Hopkins Hosp.* 1945, v. 77, 338) whereby a red Sb-dye complex is formed. By this means, 0·5 microgramme of the element could be estimated in the absence of iron. Towards the end of treatment, the level in plasma was approximately 100 microgrammes per litre after both drugs. Twenty-eight days later, only one-fifth of that amount was present. The concentration in red cells was consistently higher than in plasma. The urinary excretion towards the end of treatment was somewhat higher after Fouadin, being then approximately 10 mgm. per day and 2 mgm. daily in faeces. Antimony was still detectable 100 days later in both excretions. A small concentration of Sb was present in bile. Of 33 patients treated with Fouadin, 82 per cent. who remained under observation had ova in their faeces 3 months later and a similar percentage were passing ova after a second course. The relapse rate was 19 per cent. in 59 patients after a course of tartar emetic.

J. D. Fulton

WRIGHT, W. H., BAUMAN, P. M. & FRY, N. **The Control of Schistosomiasis Japonica. VI. Studies on the Chemical Impregnation of Uniform Cloth as a Protection against Schistosomiasis Japonica.** *Amer. J. Hyg.* 1948, Jan., v. 47, No. 1, 33–43.

These studies were carried out by members of the Commission on Schistosomiasis, Army Epidemiological Board, United States Army. Studies Nos.

I, II, III, and IV, have already been noted in this *Bulletin*, while No. V has not yet been published.

The experiments and observations recorded in Study No. VI were designed to ascertain if some method could be found for impregnating the socks and trousers of combatant troops in order to afford protection to the lower parts of the body which in combatant operations, would be most exposed to the danger of infection by cercariae. The experiments were carried out with various types of Army cloths, which were soaked in the chemical to be tested, and then wrung out and subsequently dried. After each test, the cloths were washed, with a rather more thorough technique " than is usually employed by the average enlisted man ", to ascertain if any effectiveness had been dissipated through the washing process. Each stage in the process of impregnation and subsequent washing was carried out under carefully standardized conditions, which included calculations on the amount of the chemical taken up by the treated cloth. The resistance to penetration by cercariae of the impregnated cloths, was ascertained before and after each washing, by experiments with animals ; but, owing to the large number of drugs submitted for testing, and the relatively few suitable animals available, preliminary screening by *in vitro* tests was necessary. For this purpose, a measured piece of the previously impregnated cloth was placed in a Petri dish, together with 4 cc. of water, for 10 minutes ; 10 cercariae were then added to the fluid, and kept under observation for 30 minutes. Those compounds which showed the highest percentage of kill were selected for the animal tests, which were of two types. In the first, the impregnated cloth was stretched tightly over a small wire basket, and the animal was placed in this cloth-covered basket, which was then stood on raised supports in a vessel containing 600 ml. of water, to which 3,000 to 5,000 *S. japonicum* cercariae had previously been added ; under these conditions, about 200 ml. of the water in the bath penetrated the cloth. Exposure was for 45 minutes, and samples were taken from inside the cloth after 20, 30, and 40 minutes, in order to determine whether the cercariae had penetrated. In the second method, test and control animals were anaesthetized, and a small amount of water containing 500 shed cercariae was made into a pool on the cloth to be tested, which was applied directly to the shaved surface of the animal's abdomen. After 45 minutes' exposure, the cloth was removed and the animal kept under observation for 28 days or longer, after which it was destroyed and examined for *S. japonicum*. In addition to these tests of impregnated cloths, the writers carried out a limited number of experiments with untreated uniform cloth, and with certain types of water-repellent garments issued to the troops.

The authors summarize their results as follows :—

" To determine the value of impregnated clothing as a protection against the acquisition of schistosomiasis japonica, in vitro and in vivo tests were carried out with 31 compounds or combinations of compounds. Types of uniform cloth tested included 8·2-ounce cotton suntan trouser cloth, herringbone twill cloth, olive drab woolen trouser cloth, cotton gloves, and cotton socks. A total of 537 animals was utilized in the exposure tests. A number of the compounds were discarded after in vitro screening tests while others failed to give good protection on the animal tests.

" An emulsion of 4·5 per cent. benzyl benzoate with 0·5 per cent. Tween 80 in water proved to be the most effective compound. Cotton trouser cloth and herringbone twill cloth impregnated with this emulsion provided protection through 4 washings of the cloth. Dibutyl phthalate in a 5 per cent. emulsion with Tween 80 in water afforded protection with cotton trouser cloth, herringbone twill cloth, and olive drab woollen trouser cloth after two washings of each

type of cloth. There is reason to believe that this compound might be equally effective or more effective than benzyl benzoate. Good results were obtained also with the gas protective chemical, CC_2 [this is not a chemical formula, but a secret designation]. This compound protected through two washings of herringbone twill, cotton glove material, and cotton socks. Since the latter fabric is easily penetrated by schistosome cercariae, the protection afforded by the chemical is of considerable significance and indicates that it might persist even after additional washings.

"The impregnation of clothing with certain water repellent compounds gave good results in some instances. However, this protection was gradually lost when the cloth was washed. In general, such compounds gave results inferior to those obtained with miticidal compounds.

"The relative degree of protection afforded by various types of uniform cloth varied with the weave of the cloth and the amount of the chemical taken up during the impregnation process. From a practical standpoint, impregnated woolen uniform cloth would provide protection over a longer period of time and after more washings than either the cotton suntan or the herringbone twill cloth. The latter would appear to offer the least protection against schistosome cercariae of the 3 standard types of uniform cloth." *R. M. Gordon*

WRIGHT, W. H., BAUMAN, P. M. & FRY, N. **The Control of Schistosomiasis Japonica. VII. Studies on the Value of Repellents and Repellent Ointments as a Protection against Schistosomiasis Japonica.** *Amer. J. Hyg.* 1948, Jan., v. 47, No. 1, 44–52, 1 fig.

The experiments recorded in this paper were designed to supplement the cloth-impregnation experiments described in the previous paper, and to develop a method for protecting the unclothed parts of the body against schistosome cercariae. Liquid preparations, although they protected when applied undiluted and allowed to dry on the skin, proved less satisfactory than the various ointments, which were used in 46 experiments on 348 mice exposed to infection with the cercariae of *S. mansoni* and *S. japonicum*. In the case of animals exposed to *S. mansoni*, the vertical immersion of the rodent's tail in water proved satisfactory, but, owing to its surface-haunting habits, other methods, which are fully described by the authors, had to be used in the experiments with *S. japonicum*. "All of the ointments employing dimethyl phthalate, dibutyl phthalate, benzyl benzoate, Rutgers 612, Indalone, or 2-phenylcyclohexanol, either singly or in combination in various types of bases, protected all of the experimental mice with the exception of the ointment containing copper silicate, dimethyl phthalate, and Rutgers 612 and the ointment containing 5 per cent. of dimethyl phthalate and 5 per cent. of Rutgers 612. . . . Copper silicate alone also failed to protect, although copper acetate 2 per cent. afforded protection against infection, as did a combination of copper acetate 1 per cent., dimethyl phthalate 5 per cent., and Rutgers 612 : 5 per cent." Two of the ointment bases in themselves offered little resistance to the cercariae, so that the protection conferred by the repellent ointments is not merely mechanical. It is clear from the results of these carefully conducted experiments that certain of the repellent ointments which were tested are of considerable value in protecting individuals exposed to schistosomiasis. The authors point out, however, that many additional tests are needed, particularly as regards the length of time such ointments remain effective during continuous exposure to water, or under conditions causing copious perspiration.

R. M. Gordon

ORLANDI, A. Ricerche sistematiche sull'anchilostomiasi nella popolazione rurale di Milano. [**Ankylostomiasis among the Rural Population of Milan.**] *Rass. Med. Indust.* Torino. 1947, July–Sept., v. 16, No. 3, 102–39, 9 figs.

After a few introductory paragraphs on the history of *Ancylostoma*, the author presents tables showing the returns at the Maggiore Hospital from 1914 to 1942 and at the Industrial Diseases Clinic from 1911 to 1942, and cases notified in Milan between 1929 and 1942. There follows an account of Milan itself, its position, climate, soil, water-supply and irrigation system, the character of the buildings and the population. Most of this is not of much general interest. Milan has an area of 18,174 hectares and a population of 143,535, of which 71,295 are males and 72,240 are females. Examination was made of the faeces of 37,975 persons and 2,675 (7 per cent.) were infested with hookworms, 5,253 (14 per cent.) with *Ascaris* and 9,541 (25 per cent.) with *Trichuris*; 927 (123·4 per 1,000 children under 14 years of age) were infested with *Hymenolepis nana*.

Of those with ankylostomiasis, 1,152 were males (60 per 1,000 examined) and 1,523 (179·8 per thousand) were females. Up to the age of 24, men and women work equally in the market- and kitchen-gardens and the infestation is about equal, but between the ages of 24 and 54 women are employed thus in far higher nunbers and they work in them barefoot; thus is explained the greater number of females infested. In another table, in which the occupations of over 2,000 infested persons are given, the figures for 778 engaged in horticulture (including cultivation of fruit) were 167 males, 611 females. The densities of population in 6 rural zones and of 42 localities in these zones at which persons were examined are tabulated, and detailed results are presented of each of these. The details there given show how the total examined and the numbers positive, above stated, are made up.

The common clinical symptoms were: Rise of temperature to just over 38°C. (occasionally to 39·5°) was frequent; also bronchial catarrh, but this could not be definitely ascribed to the infestation; flatulence and gastric pain were complained of by about half the patients and palpitation and dyspnoea with rather low blood-pressure readings. Eosinophilia averaged about 10 per cent., with total leucocyte counts ranging round the normal. In the early stages, itching with papular or vesicular rash was present in nearly all. Treatment for a normal subject of 70 kgm. was daily administration of three keratin-coated capsules of tetrachlorethylene (0·6 cc. each) fasting, and avoiding during the day fatty foods and alcohol. On the third day, the capsules were followed, at an interval of half-an-hour, by a magnesium sulphate purge in "abundant water", no food being allowed till the purge had acted. Flatulence and slight vertigo and mental hebetude (*intontimento*) were observed in some patients soon after the drug was taken. Of 2,543 so treated, 1,821 (71·61 per cent.) were cured by one administration [? one course of three-day treatment]; 651 (25·68) more by two administrations and 71 (2·71 per cent.) after the third.

H. Harold Scott

BACIGALUPO, J., TREPAT, L. & RAUL ETCHEGARAY, E. Dermatosis lineal por larvas de nematodes (Larva migrans). [**Creeping Eruption due to Nematode Larvae.**] *Semana Méd.* 1948, Feb. 19, v. 55, No. 8, 290–96, 8 figs.

A discussion of 11 cases published in the Argentine. The larvae were not identified, but it is believed that most of the cases were due to the larva of *Ancylostoma brasiliense*. *H. J. O'D. Burke-Gaffney*

DEL MUNDO, F., BALTAZAR, Susana, SUCGANG, Ester & PALARCA, Emilia. **Ascariasis in Children and the Response to Hexylresorcinol.** *J. Philippine Med. Ass.* 1947, Dec., v. 23, No. 12, 601–4.

The authors, in the Philippines, treated 331 children suffering from ascariasis with hexylresorcinol: the drug was administered in the form of crystoids and 0·1 gm. was given for each year of age.

Most of the cases occurred in children under 4: of 347 children originally observed, 145 were between 1 month and 4 years. In 75 cases, *Ascaris* was expelled by the mouth and in 23, by the rectum. The predominant manifestations are shown in a table, which reveals that abdominal pain and vomiting were the commonest. It is noted that voracious appetite was only recorded in 2 cases and that anorexia, on the contrary, occurred in 14. In 12 cases, a diagnosis of an acute abdominal condition was made, and, in fact, in one case, acute appendicitis was also present, requiring surgical intervention. All the other 11 such cases responded to conservative treatment and to hexylresorcinol; and the patient who had had the appendix removed also responded thereafter to this drug.

Only 13 patients showed untoward effects of the drug [in the summary, this is given as 6]: 6 had first-degree burns of the buccal mucosa and adjacent skin from crushing of the crystoids; the burns healed readily. Increased abdominal pain and nausea each occurred 3 times and lassitude once.

Of the total of 331 patients treated, *Ascaris* was expelled in 251 (75·8 per cent.). In most cases, the worms were expelled within 24 hours: in one group of 152 cases, 108 expelled the worm within this period and all but 3 expelled them within 48 hours.

In 30 cases, the number of worms expelled could not be counted and in 7 "balls of ascaris were passed out." The number of *Ascaris* expelled was, proportional to the degree of infestation rather than to the dose of the drug.

The authors consider that the ease of administration makes this treatment satisfactory. They draw attention to the need for careful diagnosis of cases suggesting an acute surgical condition and the desirability of observing such cases in hospital. [A form of medication which is liable to result in first-degree burns of the buccal mucosa, even by accident, in 2 per cent. of cases would appear to require some modification.] *H. J. O'D. Burke-Gaffney*

KIRK, R. **Observations on Onchocerciasis in the Bahr-el-Ghazal Province of the Sudan.** *Ann. Trop. Med. & Parasit.* 1947, Dec., v. 41, Nos. 3/4, 357–64. [11 refs.]

The vector of onchocerciasis in the Sudan is *Simulium damnosum*, which is widely distributed; in the Bahr-el-Ghazal it has a well-marked seasonal incidence, being most prevalent from June to August. For diagnosis of the infection, small skin sections were cut with a razor and impression smears were made of the tissue fluid from the cut surfaces. These were dried and later stained with Leishman's stain. This technique was satisfactory and convenient. At Basia, near Yambio, out of 800 persons examined, 160 had nodules and 65 had skin abnormalities which might have been due to *Onchocerca*; of these 65 persons, 33 showed onchocercal microfilaria in smears. Of these 33 positive cases, 10 had nodules, 20 had skin abnormalities and 5 were blind or nearly blind. At the Sueh rest-house near Tembura (640 persons examined) 40 persons had suggestive skin conditions and 88 per cent. of these contained microfilariae, while of skin smears from 44 apparently normal persons, 77 per cent. contained

microfilariae. The results of surveys made in this and other places are shown in the table.

Locality	Positive skin smears, per cent.	Nodules, per cent.	Blindness, per cent.
Sueh Rest-house	80	3·4	Under 1
Raffile-River Bo	76	42	4–5
Raffile-Peili ...	50	20	This probably includes all three localities
Peili	25	3	
Pongo	90	46	10
Wau	19	—	Reported low

The number of persons examined was usually between 30 and 80. The nodules were mostly on the side of the chest or near the iliac crests and great trochanters, but many patients had no nodules. The skin conditions included xerodermia, and a condition like craw-craw. Blindness occurs and is definitely due to onchocerciasis in some cases ; it is often preceded by a period of night-blindness. Hydrocele and scrotal elephantiasis are extremely common in the areas of onchocerciasis in the Sudan, but *W. bancrofti* infection is extremely rare. *F. Hawking*

MAZZOTTI, L. & HEWITT, R. Tratamiento de la oncocercosis por el cloruro de 1-dietilcarbamil-4-metilpiperazina (Hetrazan). [**Treatment of Onchocerciasis by Hetrazan.**] *Medicina*. Mexico. 1948, Jan. 25, v. 28, No. 548, 39–42.

The authors, following up the success recorded by SANTIAGO-STEVENSON and his colleagues in filariasis due to *W. bancrofti* [this *Bulletin*, 1948, v. 45, 353] have tried Hetrazan (1-diethylcarbamyl-4-methylpiperazine) in 6 patients infected with *Onchocerca*, in doses of 2 mgm. orally per kilo body-weight, thrice daily. Four took it for 15 days and two for 21 days. Cutaneous biopsy was made thrice a week for 45 days and thereafter twice weekly. Before the treatment was begun, microfilariae were numerous, as many as 60 in a specimen 6 mm. square. Within 24 hours of beginning the treatment, four patients showed a generalized oedema, especially of the face and upper part of the chest, with fever, general malaise, pruritus and joint pains. In these cases the drug was suspended for 3 days, by which time these symptoms had disappeared ; they were regarded as allergic. Microfilariae were much fewer, even after 24 hours. Biopsies during the next 6 weeks revealed : in patient No. 1, one microfilaria on the 17th day ; one in No. 2 on the 14th day ; 5 in No. 3 between the 5th and 8th days. This patient had to leave hospital on the 17th day and on that day 6 cutaneous biopsies were carried out and all were negative. No. 4 showed 3 microfilariae on the 6th day.

The other two patients were given one-third the dose on the first day, two-thirds on the second day and thereafter the full dose for 21 days. After 48 hours and during 90 days' observation, an occasional microfilaria only was seen. One of these patients had three nodules which were later extirpated ; Nos. 1, 3 and 4 also had nodules which, when removed from 14 to 39 days after the drug treatment was started, were found to contain adults normal in appearance, and living embryos. In one nodule, the adults seemed to be normal, but microfilariae, which were present in large numbers, were all dead. [See OLIVER-GONZÁLEZ & HEWITT, below.] *H. Harold Scott*

ALICATA, J. E. & KARTMAN, Anna Y. **Incidence of Oxyuriasis among a Group of School Children in Honolulu.** *Hawaii Med. J.* 1948, Jan.–Feb., v. 7, No. 3, 214–15, 2 figs.

"An examination of a group of 138 children, aged 2½ to 7, attending school (nursery to first grade) in Honolulu, showed 31·1 per cent. to be positive for pinworms on two swab examinations. Calculated on the basis of seven swabs, believed required to reveal most cases, the incidence of infection would probably be about 38 per cent. The number of positive cases was found to be equal among the two sexes. Children of Caucasian ancestry appeared to show a higher incidence of infection (40 per cent.) than those of Oriental ancestry (21 per cent.). The results indicate that oxyuriasis is probably common in this community and represents one of the problems of public health importance."

OLIVER-GONZÁLEZ, J. & HEWITT, R. I. **Treatment of Experimental Intestinal Trichinosis with 1-Diethylcarbamyl-4-Methylpiperazine Hydrochloride (Hetrazan).** *Proc. Soc. Exper. Biol. & Med.* 1947, Oct., v. 66, No. 1, 254–5.

Since Hetrazan has been used with good results in filariasis [this *Bulletin*, 1948, v. 45, 353], it was considered worth testing it in *Trichinella spiralis* infections in white rats.

Between 1,000 and 1,300 *Trichinella* larvae were given by stomach tube and 24 hours later a course of Hetrazan was started; a dose on the basis of 200 mgm. per kilogramme body-weight was given by stomach tube 3 times a day for 5 to 10 days. Rats were killed after 5, 10 and 30 days and the intestines and muscles were examined for worms and larvae.

After 5 days, an average of 91 worms were recovered from the intestines against 481 in the case of untreated controls. After 30 days the average number of larvae recovered from the muscles in the two groups of untreated animals was 31,200 and 26,100 compared with 320, 112 and 2 in three groups of animals treated for 5,10 and 20 days, respectively.

Hetrazan is relatively non-toxic in man and it is thought possible that, as in the case of filariasis, the effective dose in man may be lower than that required in the rat.

[In the table, it is shown that after 10 days 312 worms were recovered from the intestine of the treated rats against 61 in the untreated rats: there is no comment in the text on this apparently paradoxical observation.] [See also MAZZOTTI & HEWITT, above.] *L. E. Napier*

DEFICIENCY DISEASES

MACNAMARA, O. D. **The Effect of Diet and Helminthic Treatment on African School Children.** *Trans. Roy. Soc. Trop. Med. & Hyg.* 1948, Jan., v. 41, No. 4, 519–24.

The African child in central Nigeria is undernourished, and usually suffers from helminthic infection—most commonly hookworm and urinary bilharzia. One hundred and sixty-five school-children were divided into 3 groups: a control group received no treatment of any kind: a second group was given extra food at school; the supplement was calculated to produce an adequate and well balanced diet: a third group was treated for helminths with oil of chenopodium and tartar emetic. The period of observation was 100 school days. The group which had extra food showed an average weight gain of 3 lb. 10½ oz.,

compared with 1 lb. 10½ oz. in the control group, and 9½ oz. in the group treated for worms. There was no significant difference between the groups in the gains in height. In the supplemented group, there was a significantly greater increase in chest circumference, and an increase in endurance, as tested by hanging from a bar. General health was also better in this group, and signs of vitamin deficiency disappeared. There was no improvement of general health in the group given antiparasitic treatment. *J. C. Waterlow*

REID, J. A. & WILSON, T. **Report on Nutrition, and Discussion of the Main Causes of Death, "F" Force, Thailand.** *J. Roy. Army Med. Corps.* 1947, Oct.; v. 89, No. 4, 149–65.

The story of "F" Force, Thailand, is now fairly well known. As a result of appalling living conditions, forced labour, cholera, dysentery, malaria and deficiency disease, 44 per cent. of the force of 7,000 men died in a year. Anyone who reads this paper must feel admiration for the authors and those who worked with them; when it must have seemed unlikely that any of them would ever return to civilization, they continued to collect data and to keep records in face of immense moral and material difficulties.

Major Reid and Captain Wilson give a general description of the conditions to which "F" Force were exposed, but their chief emphasis is on nutrition. The diet issued by the Japanese consisted mainly of highly-milled rice, with some dried beans. Meat, when provided, was usually in a state of decomposition. Supplements were almost unobtainable, but in some camps green leaves and wild gourds were eaten. Analysis of the diet shows that 80 per cent. of the energy was derived from carbohydrate, and 90 per cent. of this from highly milled rice. The protein intake was in the region of 30–50 gm., mainly of vegetable origin. Fat and vitamin A were almost completely absent. The average daily amounts of vitamin C, riboflavin and nicotinic acid were about 3, 0·7 and 6 mgm. respectively. The thiamin : non-fat-calorie ratio [the total amount of thiamin in the diet (μgm.) divided by the non-fat calories] never exceeded 0·3, and was usually below 0·24. The value given by WILLIAMS and SPIES as the minimum necessary to protect against beriberi is 0·3. It is not surprising that under these conditions beriberi was widespread, and accounted for 13 per cent. of the deaths: 11 per cent. more were attributed to beriberi complicated by dysentery. The diagnosis of beriberi was based mainly on the presence of oedema, which was almost universal. Acute cardiac beriberi was common, but the dry neuritic type was rare.

Another very common condition, attributed to malnutrition, was tropical ulcer. The cases improved, and were less frequent, when rice polishings became available. A most important observation was the rarity of diseases caused by deficiency of the B_2 vitamins, such as scrotal dermatitis and glossitis, painful feet, paraplegia and amblyopia. Many of the members of "F" Force had suffered from these conditions while in Changi. Men who had glossitis or scrotal dermatitis when they left Singapore recovered on the train journey, or soon after reaching Thailand. The suggestion has been made that in some way this may be related to the low calorie intake. BURGESS in Singapore [this *Bulletin*, 1947, v. 44, 114] observed that signs of riboflavin deficiency appeared mainly in the relatively well-nourished.

The authors state their conclusions as follows: "In our opinion—and we think it is shared by every M.O. on this expedition—the gross inadequacy of the Thailand diet . . . in conjunction with the merciless compulsion to excessive exertion, outweighed in importance all other causes of death."

[This opinion is of value, since there are still many parts of the world where the population is exposed to similar, if less serious, conditions of malnutrition

and disease. Any experience is important that indicates where to attack the vicious circle that these, acting together, so easily set up. In the case of "F" Force, it is permissible to speculate that some of the cases of diarrhoea, diagnosed as dysentery, may in fact have been caused by malnutrition. (See McKenzie, this *Bulletin*, 1940, v. 37, 809).] *J. C. Waterlow*

Epstein, S. **Observations on Beriberi Heart Disease.** *Amer. Heart J.* 1947, Sept., v. 34, No. 3, 432–40, 5 figs. [23 refs.]

A case is described of a middle-aged woman, who for many years had been living on large amounts of alcohol and very little food. On admission to hospital she had signs of congestive heart failure and a macrocytic anaemia with achlorhydria. Both conditions responded to treatment with vitamins and a full diet.

The diagnosis of beriberi was based on the following evidence:

1. the dietary history;
2. the presence of signs of malnutrition (glossitis, cheilitis) but not neuritis;
3. the presence of cardiovascular changes considered to be characteristic of beriberi: enlargement of the heart, increased output, pistol-shot sounds, raised venous pressure and low voltage in the electrocardiogram;
4. the response to treatment, described as specific: 100 mgm. of thiamin, 150 mgm. of nicotinic acid, and 200 mgm. of ascorbic acid were given daily, together with vitamins A and D, blood transfusions and a full diet.

[In recent years, workers in America have attempted to define criteria for the early diagnosis of cardiac beriberi (see Blankenhorn, *et al.*, this *Bulletin*, 1946, v. 43, 945). This is difficult, because the cardiovascular changes are not specific. In the case described above they could, as the author admits, be attributed to anaemia—an explanation which is not ruled out by the fact that the condition of the heart improved before that of the blood (see Hunter, A., *Quart. J. Med.*, 1946, v. 15, 107). In the present state of knowledge there seem to be only two convincing tests for beriberi: a dramatic response (within a few hours) to parenteral administration of thiamin; and an increase in pyruvic acid in the body fluids, either at rest or after mild exercise (see Lu and Platt, *Biochem. J.*, 1939, v. 33, 1538).] *J. C. Waterlow*

SPRUE

Cooke, W. T., Frazer, A. C., Peeney, A. L. P., Sammons, H. G. & Thompson, M. D. **Anomalies of Intestinal Absorption of Fat. II. The Haematology of Idiopathic Steatorrhoea.** *Quart. J. Med.* (n.s.) 1948, Jan., v. 17, No. 65, 9–24, 2 figs. on 1 pl. [65 refs.]

This paper represents a study of the haematology of 45 cases of idiopathic steatorrhoea, and contains observations on the aetiological factors concerned. Diagnosis has been made on the history, the presence of a characteristic haematological and abnormal electrolyte picture, excess faecal fat, flat glucose and chylomicrograph curves and low fasting serum lipoids.

In 42 patients, the presence of a fat absorption defect was determined by a fat balance technique. Most hypotheses concerning the anaemia in idiopathic steatorrhoea have been based upon the unitarian theory of the aetiology of the macrocytic anaemias, but the similarity between the anaemias of steatorrhoea and pernicious anaemia are superficial and a close relationship between them could not be established in this series. Although minor differences may be seen

in the morphology of the peripheral blood and in Price-Jones curves, more significant differences are in the high incidence of free hydrochloric acid in the gastric contents and the demonstration of intrinsic factor in the gastric juice of one patient. Furthermore, refined liver extracts did not produce a reticulocyte response in the blood picture, even in those presenting sternal marrow findings identical with those in pernicious anaemia.

Minor degrees of iron-deficiency were remedied in some, but the finding of a low colour index or low mean corpuscular haemoglobin concentration was not an indication that such blood pictures could be corrected by administration of iron alone. A consistent feature has been decreased fragility of red cells to hypotonic saline, similar to that noted in a number of anaemias. The rapid fall in red cells and haemoglobin that may occasionally be noted suggests a haemolytic process comparable with that demonstrated in pernicious anaemia, and the finding of increased erythropoiesis in the bone-marrow with relatively static peripheral blood counts might also be regarded as evidence of a maturation defect.

Serum-bilirubin levels have not been markedly abnormal. Total pigment excretion in the urine and faeces was within normal limits. There is therefore little evidence of increased red cell destruction in idiopathic steatorrhoea.

The conception that faults in fat absorption may give rise to blood disorders opens up wide fields of investigation. The lack of correlation between the haematological improvement and the fat absorption defect and the occurrence of death with a relatively normal blood picture might be considered as evidence against the anaemia being secondary to the underlying fat absorption defect. It can be shown, however, that there are aetiological differences between the various types of defect. Thus the absorptive defect persists in idiopathic steatorrhoea, whereas in sprue and pellagra the defect may disappear entirely. It seems that qualitative changes in fat absorption may occur in the absence of any alteration in the total amount of fat absorbed. It may be, as is suggested by the recent demonstration of the action of folic acid and thymine, that the reticulocyte responses have been due to the replacement of temporary deficiencies of various accessory factors which were conditioned by, or dependent on, an underlying fault not affected by treatment.

[For Part I see this *Bulletin*, 1946, v. 43, 946.] *P. Manson-Bahr*

i. Davidson, L. S. P. & Girdwood, R. H. **The Imbalance of Vitamins with particular reference to Folic Acid.** *Lancet.* 1948, Mar. 6, 360–63. [15 refs.]

ii. Lancet. 1948, Mar. 6, 371–2. **Folic Acid and the Nervous System.**

i. In two patients with pernicious anaemia and three with sprue who were treated with folic acid, various signs of deficiency of the vitamin-B complex arose. These signs did not improve until folic acid was supplemented with, or superseded by, liver or liver extracts. The authors, writing from the University of Edinburgh, have found neurological changes in 8 out of 20 cases of pernicious anaemia treated with folic acid alone.

The three cases of the sprue syndrome are of special interest. The first was in a patient with idiopathic steatorrhoea who developed a mild peripheral neuritis; treatment with folic acid coincided with steady deterioration of neurological features, despite improvement of assimilation from the alimentary tract, and oral and parenteral administration of large amounts of thiamine. In addition, signs of riboflavin deficiency developed. The second appeared to be a case of tropical sprue in a patient from N. Africa in whom a partial colectomy had been performed for megacolon. While the patient was undergoing folic acid treatment, signs of peripheral neuritis developed. When he was

treated with proteolysed liver by mouth supplemented with intramuscular injections of thiamin, riboflavin and nicotinic acid by the mouth, signs and symptoms of peripheral neuritis steadily improved. The third [referred to below] was a case of tropical sprue from India. On folic acid being given by the mouth, 50 mgm. daily, the intestinal symptoms responded rapidly, but within a week a fiery red rash of butterfly distribution appeared on the patient's face : cheilosis, and glossitis also occurred. There was severe mental depression. No response was obtained to nicotinic acid, but combined therapy of folic acid and parenteral liver caused the dermatitis to subside in four days. When liver injections were discontinued, the dermatitis recurred, but it disappeared when folic acid was discontinued. The implications of this curious anomaly and the possible underlying principles have already been discussed.

ii. One of the surprises of treatment with folic acid has been the complete failure of this anti-anaemic substance to influence the changes in the nervous system that occur in many patients with pernicious anaemia.

It is possible, as HURST argued, that changes in the haemopoietic and nervous systems are due to deficiencies of different factors, both in some way connected with achlorhydria. In support of this, it is to be noted that some patients with pernicious anaemia have no detectable involvement of the central nervous system, and others with combined tract degeneration of the spinal cord who show no anaemia. But even this does not explain why these nerve changes should appear in those whose blood has been restored to normal by folic acid. This acute cord involvement is something quite new. But when the correct treatment with liver is substituted, recovery of the nervous system is quicker than is normal in the naturally occurring combination of pernicious anaemia with postero-lateral cord sclerosis. Some have even suggested that folic acid may in some way interfere with the metabolism of the conducting tissue of the nervous system.

For the curious action of folic acid in reproducing pellagrous symptoms, including dermatitis in a sprue patient reported by DAVIDSON and GIRDWOOD [above], different explanations are suggested.

In the United States, ROSS, BELDING & PAEGEL, (*Blood*, 1948, v. 3, 68) observed that, on the whole, the patients who exhibited signs of posterolateral tract disturbance were those receiving the larger doses and that it persisted as long as folic acid was taken. Is it possible that folic acid denies to the nervous tissue an essential substance, in much the same manner as sulphonamides block the utilization of *p*-aminobenzoic acid in bacterial metabolism ? Davidson and Girdwood think that treatment with one member of the vitamin B complex may sometimes bring out signs of deficiency of others ; and that disproportion of vitamin B members might be responsible for the appearance of peripheral neuritis and of pellagrous symptoms in steatorrhoea and that some similar mechanism might explain damage to the posterolateral tract during treatment of pernicious anaemia with folic acid. Liver extract may act by " liberating " the appropriate vitamins from " conjugated " forms.

At the present moment, the hypothesis of Ross *et al.* in the United States appears the most likely, as the Edinburgh series of cases of steatorrhoea had possibly multiple deficiencies. The connexion between subacute combined cord degeneration and vitamin B deficiency is not proved, as was shown by Spies's patients with nutritional anaemia who were kept on a deficient diet and treated with folic acid (SPIES *et al.* this *Bulletin*, 1948, v. 45, 462).

The lesson is clear—namely that, whether alone or with liver extract, folic acid must not be given to patients who show any signs of involvement of the nervous system, and the idea that folic acid and liver extract together are preferable to liver alone is negatived. [See also this *Bulletin*, 1948, v. 45, 360.]

P. Manson-Bahr.

JUKES, T. H. & STOKSTAD, E. L. R. **Pteroylglutamic Acid and related Compounds.** *Physiol. Rev.* 1948, Jan., v. 28, No. 1, 51–106, 3 figs. [306 refs.]

HAEMATOLOGY

ESTES, J. E., FARBER, E. M. & STICKNEY, J. M. **Ulcers of the Leg in Mediterranean Disease.** *Blood.* 1948, Mar., v. 3, No. 3, 302–6, 2 figs.

"Ulceration of the skin of the legs may occur in Mediterranean disease [Cooley's anaemia]. Such ulceration cannot be distinguished grossly from that occurring in sickle cell anemia and congenital hemolytic icterus. The outstanding histologic feature (noted at biopsy of one of these ulcers) is the prominent deposition of iron in the cutis."

SLATEN, E. F. **Familial Erythroblastic Anemia (Cooley's Anemia). Report of Possible Cases in Two Filipino Brothers.** *Hawaii Med. J.* 1948, Jan.–Feb., v. 7, No. 3, 210–13, 1 fig. [18 refs.]

DA SILVA, E. M. **Absence of Sickling Phenomenon of the Red Blood Corpuscle among Brazilian Indians.** *Science.* 1948, Feb. 27, 221–2. [11 refs.]

VENOMS AND ANTIVENENES

MOLE, R. H. & EVERARD, A. **Snake-Bite by** *Echis carinata.* *Quart. J. Med.* 1947, Oct., New Ser., v. 16, No. 64, 291–303, 2 figs. [20 refs.]

This is an account of clinical and laboratory findings in two cases of snake bite treated in the R.A.F. General Hospital, Karachi. The snake responsible for the bite was not positively identified in the first case, although strong circumstantial evidence is provided that it was *Echis carinata.* This snake was identified in the second case.

The first patient was bitten in the right ankle and did not report until 8 hours later, by which time the right foot and leg up to the knee were swollen and "patchily discoloured by extravasated blood." The popliteal pulse was not palpable. The patient collapsed after the intravenous administration of 5 cc. polyvalent antivenom serum (Kasauli). His condition deteriorated and by the second day the coldness and pulselessness of the affected foot suggested that gangrene was developing. Expectant treatment was carried out, and in view of continued haemorrhages (urine and faeces both contained blood) blood transfusion was started. The patient improved but on the fourth and fifth days, although the circulation in the right leg had improved, haemorrhages from the various skin lesions and into the urine became increasingly profuse. At this stage, as on the second day, blood platelets were almost absent. He subsequently had two attacks of pallor and restlessness which were considered to be due to pulmonary infarcts, and suffered two extensor spasms of the limbs and trunks, but on the sixth day he improved and the bleeding stopped suddenly. An hour later transfusion was stopped. Blood was present in the urine until it disappeared suddenly on the eighth day. Convalescence was interrupted by a mild paranoid state.

On the second day, the platelets were too few to count and plasma fibrinogen was reduced to less than 10 mgm. per cent. Clotting time of venous blood was greatly increased over normal and the clot showed only a few "tiny fibrin

strands." The icteric index was 11. The platelet count was still very low on the third day, but after that began to improve. By the fifteenth day, both the platelet count and the fibrinogen content of plasma were normal. The icteric index rose to 22 on the sixth day and was 12 on the fifteenth. The haemoglobin percentage was 96 on the second day, 70 on the third, 75 on the sixth and thereafter rose to normal.

Benzoate detoxication tests were carried out on three occasions in the first case over the second three weeks of the illness. The results indicated " prolonged impaired hepatic function ". Similar tests on the third day demonstrated considerable reduction in excretion of hippuric acid ; this was still evident to a much less marked degree on the 20th day.

The second patient was bitten in the thumb. The snake was killed and identified. The bite wound was incised and an intermittent tourniquet applied to the arm within 15 minutes. Half an hour later, 10 cc. polyvalent antivenin (? Haffkine) was administered intravenously. Five hours after the bite, the patient complained of abdominal pain and retching. A further dose of antivenin was given and blood examinations were made. Recovery followed, but convalescence was slow. Six hours after the bite, the plasma fibrinogen was normal but there were too few platelets to count. Eight hours later, platelets numbered 15,000 per cmm., and thereafter returned to normal by the third day.

The authors suggest that *Echis* venom has a pronounced effect on liver function and on " capillary function ", as illustrated by the haemorrhages and thrombocytopenia. Because in the first patient the bleeding into the urine continued for two days after bleeding from other sites had stopped, they suggest that the venom is excreted by the kidneys. In spite of increased clotting time, they regard venous thrombosis to be the cause of the " intensity of the oedema and absence of any detectable circulation ", in the affected limb in the first patient. No fibrolysin was detected, so that the lack of fibrinogen was probably related to failure of production in the liver. The platelets were probably being produced in normal numbers, but " were consumed in some way directly or indirectly by the action of venom."

In discussing treatment, the authors stress the importance of administration of antivenin. Continued blood transfusion is recommended in order to maintain blood volume. They advise forcing fluids by mouth to induce a high urinary output, hoping in this way to assist in the elimination of the venom.

[The important point made in this paper is the emphasis on the value of early and continued blood transfusion. It is a pity that the snake was not identified in the first case. The arguments advanced in support of the view that the venom is excreted in the urine are surely not valid. The evidence merely indicates severe damage to the renal vessels. In any case it is unlikely that venom is excreted as such. The findings in the blood are hardly compatible with the suggestion that venous thrombosis occurred in the leg of the first patient.

The statement that " a British pathologist in West Africa . . . was bitten on the finger by a Russell's viper . . . " is remarkable in that, so far as the reviewer knows there is no other record of the presence of this species (or genus) in West Africa.] *B. G. Maegraith*

MARQVARD, H. Saenkningsreaktionen ved Hugormebid. [**Stabilizing Action of the Venom of** *Vipera berus berus* **on a Blood Suspension after Bites from the Viper.**] *Nordisk Med.* 1948, Mar. 19, v. 37, No. 12, 588–9. French (summary.)

BERGENHEM and FÅHREUS (1936) and Bergenhem (1938) have demonstrated the stabilizing power of lysocithin in a pre-haemolytic dose on a blood suspension *in vitro*. Because of its lecithase content, cobra venom has the same

stabilizing action. In 10 hospital patients, who had been bitten by *Vipera berus berus* 12 to 24 hours before, it was found that the lysocithin formed by the lecithase in the blood supensions were stabilized. It is believed that venom is the stabilizing substance. Antivenom serum given later than an hour after the inoculation of venom does not check the stabilizing action, lysocithin already formed is not adversely affected by the antivenom serum, but serum given half-an-hour after the inoculation of venom evidently restricts the action of the lecithase, because in this case the formation of lysocithin and its stabilizing action are clearly reduced. *H. J. O'D. Burke-Gaffney*

GRASSET, E. Le venin de *Bitis nasicornis*, son anavenin et préparation d'un sérum spécifique. [**The Venom of** *Bitis nasicornis* **and the Preparation of a Specific Antivenene.**] *Liber Jubilaris J. Rodhain* (*Soc. Belge Méd. Trop., Brussels*). 1947, Dec., 225–40, 3 figs. [15 refs.]

Bitis nasicornis, Rhinoceros Viper, River-Jack, the Ihele or Bata of the Belgian Congo, exists over much of tropical Africa. The author has tested the toxicity of its venom on white mice, guineapigs, rabbits and pigeons, by various routes, intravenous, subcutaneous and intramuscular. Comparing it with the venoms of *B. arietans* and *B. gabonica*, it is less toxic than either to mice and guineapigs, but to rabbits it is equal to that of *B. arietans*, but less than that of *B. gabonica*, while in pigeons the toxicity is practically the same in all three. Death is preceded by increasing dyspnoea, convulsions and, at times, the passing of bloody fluid *per anum*, and at autopsy extensive haemorrhage is seen in all the organs. Animals which survive show extensive haemorrhagic oedema, necrosis and scarring at the site of inoculation. Antivenene is obtained by injecting horses with increasing doses of anavenom (venom plus formol) and a compound antivenene can be produced by inoculating with the venoms (or anavenoms) of *B. arietans*, *B. nasicornis*, *B. gabonica* and *Naja flava*, but the antitoxic action of the compound varies considerably. For example, 1 cc. of a product thus prepared neutralized respectively of the above 22, 9·5, 22 and 2 mgm. *H. Harold Scott*

SERGENT, Et. Abris des scorpions. [**The Shelter Habits of Scorpions.**] *Arch. Inst. Pasteur d'Algérie.* 1947, Sept.–Dec., v. 25, Nos. 3/4, 206–9, 2 figs.

The author studied the types of shelter preferred by the three commonest varieties of Algerian scorpions, *Prionurus australis*, *Buthus occitanus*, and *Scorpio maurus*. In all, 11,608 observations were made.

The scorpions were studied in experimental cages, each of which was provided with a darkened and a light shelter, the latter being covered with clear glass. Each type of shelter was constructed in three different forms, namely (1) a horizontal platform, raised 3 mm. from the ground, (2) the same, resting at an angle against the side of the cage, the upper end being 4 cm. from the ground and (3) the same, with the three sides closed in with cardboard ; thus, in the case of the dark shelter, the "penthouse" was completely obscured, while the light one was illuminated by the glass plate.

It was found in this way that 90 per cent. of the scorpions preferred the dark to the clear shelter and 60 per cent. preferred the "contact" platform to the "distant" one.

This supports the findings of JEANNEL, quoted by BERLAND in his book, *Les Scorpions*, namely that scorpions, which find a refuge under stones during the daytime, like above all to have some solid body above and under them.

H. J. O'D. Burke-Gaffney

DERMATOLOGY AND FUNGUS DISEASES

BAKER, R. D. **Tissue Changes in Fungous Disease.** *Arch. Pathology.* 1947, Nov., v. 44, No. 5, 459–66.

In a comparison of the common tissue responses in fungous diseases, the author has chosen to subdivide the reactions into 5 groups, based upon the presence of suppuration, macrophages, giant cells, caseous necrosis and fibrosis. All these features commonly occur in North and South American blastomycosis, coccidioidomycosis and in sporotrichosis. In actinomycosis, nocardiosis, maduromycosis and chromoblastomycosis, similar reactions occur but without caseation. Suppuration is usually absent in histoplasmosis and in cryptococcosis. Acute inflammation with necrosis is prominent in mucormycosis and in aspergillosis. There is either no reaction or only a low-grade chronic inflammation in moniliasis or in dermatophyte infection, unless there is invasion of deep structures.

Presence of giant cells may be determined partly by the large size of fungal elements. The action of liberated endotoxins, and the development of hypersensitivity to such products, may influence cytological response. The chronicity and extent of fibrosis are partly determined by the persistence of living organisms, both free in tissues or within macrophages.

The author fails to demonstrate any one tissue change which is characteristic of fungous infection, whereas the diversity of both active and passive reactions is illustrated. *R. W. Riddell*

BAKER, R. D. **Experimental Sporotrichosis in Mice.** *Amer. J. Trop. Med.* 1947, Nov., v. 27, No. 6, 749–69, 10 figs. on 6 pls.

Groups of mice were inoculated with saline suspensions of strains of *Sporotrichum schenckii* grown on glucose agar. Intraperitoneal injection produced thin whitish plaques on the spleen and also peritoneal nodules which had increased up to 2 mm. diameter by the second week, with later peritesticular caseation. Minute grey hepatic foci appeared by the third week; sometimes the lungs were involved. Gross lesions did not change after about 4 weeks. Organisms were present in large numbers in retrosternal lymph nodes and in reticulo-endothelial cells of the liver and other organs. Haematogenous dissemination occurred in the first week. Unlike the findings in human sporotrichosis, direct examination of fresh material in 10 per cent. NaOH and in lactophenol blue, or Gram-stained smears, showed numerous organisms almost as frequently as did cultures, which were usually positive even in mice inoculated over 100 days before. Death occurred in about 3 weeks with mainly peritoneal and hepatic lesions, or was delayed until about 12 weeks when lesions were generalized.

Injection into the hind paw produced an abscess which ulcerated in the second week. Suppuration occurred in popliteal lymph nodes and osteomyelitis developed. Organisms were readily demonstrated by microscopy and culture. Spontaneous recovery was possible or haematogenous spread caused death in 2 or 3 months.

Similar results were obtained with the use of diluted pus from human sporotrichosis. The mouse, like the rat, may be used for experimental and diagnostic work, and is more readily infected than the guineapig or the rabbit.

R. W. Riddell

SANCHEZ MARROQUIN, A. & DE LOS ANGELES GONZALEZ, M. Estudio micológico de 16 casos de Esporotricosis en la ciudad de México. [**Mycological Study of 16 Cases of Sporotrichosis in Mexico City.**] *An. Escuela Nac. Ciencias Biol.* Mexico. 1945, May 15, v. 4, No. 1, 19–40, 5 figs. [Numerous refs.]

The English summary appended to the paper is as follows :—

" Sixteen cases of sporotrichosis in Mexico City are studied, classifying them in three different types ; localized lymphangitic, disseminated subcutaneous and epidermal.

" *Sporotrichum schenckii* (Hektoen and Perkins, 1900) was isolated and identified as the etiologic agent. The morphological and biochemical characteristics of the parasite are described, pointing out its particular pleomorphism and the impossibility of establishing taxonomic differences, exclusively on the basis of biochemical properties.

" Finally, biopsies of subcutaneous nodules were performed and studied in two of the cases."

LAMPHIER, T. A. **Localized Coccidioidal Osteomyelitis.** *New England J. of Med.* 1948, Jan. 29, v. 238, No. 5, 150–52, 1 fig. [20 refs.]

" A case of localized coccidioidal infection of the os calcis that did not respond to general and local therapy is presented. Amputation of the extremity was followed by highly satisfactory wound healing without further dissemination."

MENDOZA, J. T. **Histoplasmosis : Report of a Case.** *Monthly Bull. Bureau of Health.* Manila. 1947, Jan., v. 23, No. 1, 33–40, 1 folding chart.

" 1. A case of histoplasmosis, the third of this disease diagnosed in the Philippines, is reported.

" 2. The etiology and manifestations of the disease are briefly described.

" 3. It is probable that there are more cases of this disease here but they remain unrecognized due to lack of previous knowledge on its recognition. This case is therefore reported to make the local medical profession and the public histoplasmosis conscious."

HEAT STROKE AND ALLIED CONDITIONS

DAILY, W. M. & HARRISON, T. R. **A Study of the Mechanism and Treatment of Experimental Heat Pyrexia.** *Amer. J. Med. Sci.* 1948, Jan., v. 215, No. 1, 42–55, 7 figs. [22 refs.]

This paper begins with a review of the literature on heat pyrexia. From this it emerges that there are three problems as yet unsolved : why do patients stop sweating ? what is the mechanism of the circulatory collapse that is often found ? what is the most effective means of reducing the temperature ? In animals, the mechanism of evaporative cooling differs considerably from that of man, and therefore investigation of the first question—the failure of sweating—was not possible.

Cardio-vascular changes were studied in anaesthetized dogs, in a chamber heated to 45–50°C. Arterial and venous blood pressures were recorded ; the oxygen content was measured of arterial blood, and of venous blood from superficial veins, the hepatic vein and the right atrium. Total oxygen consumption

was also measured, and cardiac output was calculated by the Fick principle. As the body temperature rose, three clinical stages could be distinguished: up to about 40·5°C. (105°F.) there was increasing excitement and the skin was flushed. From 40·5° to 42°C. (105–108°F.) the flush increased and petechiae appeared; hyperpnoea was extreme; movements were poorly co-ordinated. At about 43°C. (110°F.) convulsions and coma occurred; the flush gave way to an ashen grey pallor, with depressed respiration.

As the pyrexia developed, venous pressure, measured in the right atrium, remained unchanged; arterial pressure was fairly well maintained, until the "grey" stage, when it fell to shock levels. Oxygen consumption and cardiac output rose steadily with increasing body temperature, but both fell steeply in the terminal "grey" stage. The circulation through the skin, as measured by the arterio-venous oxygen difference, increased in the initial stages, while that through the viscera was low. This suggested that cutaneous vasodilatation was compensated by splanchnic vasoconstriction. In the late stages this difference was reversed; as a result of either injury to the thermal centres or of local accumulation of metabolites, visceral vasoconstriction failed, leading to a fall in blood pressure, decreased cutaneous circulation, and death. These results indicated that the circulatory collapse caused by pyrexia was peripheral rather than cardiac.

Another series of experiments was concerned with the effects of heat pyrexia on cardiac reserve. Rats were anaesthetized, and given sudden massive intravenous infusions of saline. The venous pressure rose, but quickly fell to normal again. In rats not exposed to heat it remained normal, but in rats heated to 42–43°C. there was a secondary rise in venous pressure, followed by a fall in arterial pressure, and death. At autopsy, pulmonary oedema was found. From this it was concluded that heat pyrexia caused impairment of the cardiac reserve, and that "in patients with pre-existing cardiac disease it might be expected that heat stroke might lead to cardiac rather than peripheral failure." In mice exposed to heat it was found that moderate doses of saline given intraperitoneally increased the duration of survival. Larger and smaller doses were ineffective. Experiments with digitalis were inconclusive.

The effectiveness of treatment was investigated in rats and mice. The animals were heated to the point of coma, and then cooled. In rats, the fall in body temperature was followed by means of a thermometer inserted in the large intestine; in mice the efficiency of the treatment was estimated by the number of mice surviving. It was found that immersion in ice-water produced more rapid cooling, and a higher survival rate, than cooling by wetting and fanning. Recommendations for treatment are given, based on these experimental findings.

[It is a pity that the limitations of animal experiments prevented the authors from extending their rigorous and careful work to the third problem—"why do the patients stop sweating?" Circulatory collapse seems to be a secondary effect of heat stroke, not a part of the condition *per se*; it is an uncommon complication in fit and young subjects, *e.g.*, in Service personnel developing heat stroke in India or Iraq. In these patients, treatment by wetting and fanning in a cool room has proved effective, even if it does not produce the most rapid cooling [this *Bulletin*, 1945, v. 42, 143]. Ice-water is seldom available in large quantities in the desert. In practice the most important gap in our knowledge is not of treatment, but of prevention. This gap cannot be filled until more is known about why sweating suddenly stops.] *J. C. Waterlow*

MISCELLANEOUS DISEASES

BAUMANN, C. & GAILLARD, Blanche D. E. De practische betekenis van de functiebepaling der bloed-liquorbarrière bij neurologische patiënten in de tropen. [**Estimation of Plasma Permeability of the Choroidal Barrier in Tropical Neurology.**] *Nederl. Tijdschr. v. Geneesk.* 1948, Mar. 6, v. 92 (i), No. 10, 686–98. English summary (4 lines).

Discussion of the significance of the different composition of blood plasma and cerebrospinal fluid indicates that it is a physical and physiological phenomenon. The present article deals with this point and goes on to an argument which would explain " Tropical Headache," largely a hemicrania, as being due to increased function of the choroidal vascular plexus. The result of exposure to tropical conditions is given as increased permeability of the capillaries and an altered inorganic composition with increased tension of the cerebrospinal fluid. Estimation of the plasma quotient, or blood : cerebrospinal fluid ratio, which normally for the Walter bromide test, should be 2·9 to 3·3 is considered to support the contention and, therefore, to indicate therapy directed towards the regulation of this functional disturbance. The test is described in detail and three tables furnish the data regarding patients tested, who were soldiers present in the tropics for only a short time. [The Walter bromide test is based on the fact that the ratio of the amount of bromide in the blood and cerebrospinal fluid is constant in normal persons, but may vary in those suffering from mental disorder.] *W. F. Harvey*

DAVIES, J. N. P. **Pathology of Central African Natives. Mulago Hospital Post Mortem Studies V.** *East African Med. J.* 1947, Dec., v. 24, No. 12, 437–49. [23 refs.]

Part V of this series deals with spirochaetal diseases in Uganda. Most attention is given to syphilis and yaws, but rat-bite fever has been seen. Tick-borne relapsing fever (*Ornithodorus moubata*) has long been a scourge in Uganda, but autopsy findings are not diagnostic and spirochaetes tend to disappear soon after death. Vincent's infections are frequent as primary and secondary invaders. Their relation to tropical ulcer will be discussed in a later paper. Cancrum oris is attributed to this infection.

The incidence and characters of syphilis recorded by LAMBKIN (1909) and KEANE (1912) are contrasted with those occurring at present. The incidence is now lower and congenital syphilis is rare. Secondary syphilis is said to be infrequent [this appears to be a misinterpretation from a paper (*Brit. Med. J.*, 1947, Jan. 18, 88 ; see also this *Bulletin*, 1947, v. 44, 527) by the reviewer]. Tertiary lesions and neuro-syphilis are common [for the latter statement the author quotes from an unpublished thesis] ; so also are severe and often phagedaenic chancres. Forty years ago, the incidence was otherwise. It is suggested that the disease described by Lambkin & Keane was yaws, not syphilis despite their reports of much congenital syphilis. The author has been informed that one doctor " sees a lot of yaws—in the country round Kampala." [No mention is made of endemic syphilis, such as has been reported from other countries.]

In 2,994 autopsies (1931–1946), syphilitic lesions were recorded in 11·3 per cent. (338) ; 90 per cent. were men. In 77 per cent. of these, syphilis was the main cause of death. Aortitis accounted for 61·2 per cent. (207) ; neuro-syphilis, 44·5 per cent. (154) ; aortitis with neurosyphilis, 15 per cent. (53) ; gummata, 7·6 per cent. (26) [figures and totals do not tally]. The findings in 1946 were similar. Aortic aneurysm was present in over half of the cases of aortitis in 1946. In 190 autopsies on neurosyphilitics, 96 were found to have

G.P.I., 38 meningovascular, 5 pachymeningitis haemorrhagica and 3 transverse myelitis (in 48 there were insufficient data). The age at death for aortitis and neurosyphilis was about 40 years. Neurosyphilis is quoted as constituting 0·4 per cent. of all admissions to Mulago, which includes a Mental Hospital. Tabes is rare. Microscopically the changes in neurosyphilis of the brain are the same as those seen in Europeans. Gliomata are more frequent than intracranial gummata. In other tissues, diffuse syphilitic fibrosis and gummatous lymphadenitis were not observed.

[The author strays far from his title and wanders upon rather uncertain territory.] *C. J. Hackett*

FISHER, A. C., FISHER, Monica M. & LENDRUM, A. C. **Tropical Primary Phlebitis.** *J. Path. & Bact.* 1947, July, v. 59, No. 3, 405–15, 6 figs. on 3 pls.

This paper records a continuation of the studies first reported by FISHER [this *Bulletin*, 1942, v. 39, 199], and reference is made in it to the paper by MANSON-BAHR and CHARTERS [*ibid.*, 1946, v. 43, 1186] and to that by GELFAND [*ibid.*, 1947, v. 44, 539]. The authors think that the conditions described by these other workers and themselves are the same. Fisher writes from the Roan Antelope Hospital Service, Luanshya, Northern Rhodesia ; Lendrum from the Department of Pathology, the University and Western Infirmary, Glasgow.

They have now seen 71 cases of tropical primary phlebitis (as they now name the disease) ; of these, 7 were fatal. Two main types are defined : phlebitis major (68 cases) in which large veins are involved, and in which there is a general reaction, with fever ; and phlebitis minor, which is a lesion of small veins, easily diagnosed when the veins involved are superficial, in which general symptoms are slight. In the severe form the onset is usually sudden, with local pain, tenderness and swelling over the affected vein, and muscular spasm. There is venous engorgement distal to the inflamed area, and secondary thrombosis occurs. In milder cases there is no residual oedema (after subsidence of the acute condition in 2–3 weeks) but in severe cases the limb may be left in a condition of permanent oedema. The authors think that some of the cases of stiff neck reported by Manson-Bahr and Charters may have been due to deep-seated phlebitis. No suppuration or embolus formation has been noticed.

Of the 92 lesions reported, 34 were of the femoral vein, 8 of the popliteal, 16 of the axillary, and 7 of the subclavian vein, but other veins, including the internal (8) and external (6) jugular veins and the portal system (5), may also be involved. The disease may be fatal when cerebral sinuses or important veins are diseased, and since these veins may become involved after onset in a superficial vein, the prognosis should always be guarded.

Sulphonamides were of no apparent benefit in treatment, but the use of anticoagulants would seem to be worth trial. Illustrative cases are described.

The second part of the paper is devoted to a discussion of the aetiology and pathology of the condition. Blood culture was negative in 11 of the 12 cases in which it was tried ; in the other one *Streptococcus viridans* was isolated, but this is not thought to be a significant finding. Kahn, Widal and Weil-Felix tests were not found to be relevant ; malaria, the sickling trait and helminthic infection were not important. There was slight leucocytosis with (sometimes) moderate relative lymphocytosis.

Tissues were available for microscopic examination from several patients, and the jugular vein of one was examined in detail and under good conditions. In this there was a remarkable disruption of the normal tissues of the media and intima, with newly formed capillaries set in a loose oedematous groundwork in which there were large cells of uncertain nature, and neutrophils. The endothelial cells showed evidence of urgent proliferation ; there were other

large cells (reacting polyblasts) and in these there were cytoplasmic inclusion bodies, which were clearly demonstrated when stained by the phloxin-tartrazine method (described by LENDRUM on p. 399 of the same issue of the *Journal*). The point is made that fixation of tissues in formalin is rarely satisfactory for this purpose, and that formol-sublimate (1 part commercial formalin to 9 parts saturated aqueous mercuric chloride) should be used for 10–14 days.

The detailed description of the lesions should be read in the original. The authors point out that they may be very localized, and consequently easily missed. The changes are quite unlike those associated with bacterial infection, and the presence of inclusion bodies raises the question of virus infection, though no virus has yet been recovered. This seems to be a newly discovered disease, which occurs only sporadically in Rhodesia (though the outbreak described by Manson-Bahr and Charters elsewhere in East Africa was more in the form of an epidemic). It may be more widespread in Africa than is at present realized, and there may be cases in which obscure symptoms (for instance splenic softening or splenic abscess) are in fact due to the same cause. The method of spread is not known. *Charles Wilcocks*

CHARTERS, A. D. & MANSON-BAHR, P. E. C. **Symmetrical Gangrene in the African.** [Correspondence.] *Brit. Med. J.* 1948, Mar. 13, 520.

GELFAND [see this *Bulletin*, 1947, v. 44, 937] described 6 cases of symmetrical gangrene of the feet, in S. Rhodesia ; Charters and Manson-Bahr suggest that the aetiology of this condition may have been similar to that of thrombophlebitis [see this *Bulletin*, 1946, v. 43, 1186]. There is some similarity of early symptoms between Gelfand's cases and theirs, and gangrene due to arterial thrombosis was seen in two of their patients in whom the first signs were of phlebitis. *Charles Wilcocks*

HARRIES, E. J., LEWIS, A. A. G., WARING, J. W. B. & DOWLING, E. J. **Melioidosis treated with Sulphonamides and Penicillin.** *Lancet.* 1948, Mar. 6, 363–6, 3 figs.

The authors describe five cases of melioidosis which occurred in West African soldiers at various places between Prome and Rangoon, Burma, during 1946. Two of the cases, in which there were multiple abscesses in the liver, spleen or lungs, proved fatal in spite of treatment of one patient with sulphathiazole and of the other with various sulphonamide drugs and penicillin. It is considered unlikely that cases with multiple abscesses in the internal organs will respond to any known form of treatment.

Of the other three cases, one had superficial abscesses and two had infections involving the lungs. All recovered after combined treatment with sulphonamides and penicillin. It is known that *Pf. whitmori* is not sensitive to ordinary concentrations of penicillin, but the strain from one of the cases now reported was inhibited *in vitro* by 650 units per ml. The treatment now recommended is to give sulphamezathine 2 gm. every 4 hours for at least 10 days, and to incise all accessible abscesses or to aspirate them and instil penicillin locally. Where there is no rise in agglutinin titre, a vaccine may be used.

The suggestion that colonial roughness is associated with virulence was supported by the observation that the strains from the three patients who recovered were noticeably less rough than the others.

The reports also indicate that an agglutinin titre of 1/80 is likely to be significant and a titre of 1/160 almost certainly diagnostic of melioidosis.

J. C. Cruickshank

ENTOMOLOGY AND INSECTICIDES: GENERAL

MUESEBECK, C. F. W. **Common Names of Insects of Medical Importance approved by the American Association of Economic Entomologists.** *Mosquito News.* 1947, June, v. 7, No. 2, 70–72.

This is a short list of insects, classified in two forms: 1. By the common names with the scientific names appended (*e.g.*, American dog tick—*Dermacentor andersoni*), and 2. *Vice versa*.

Its importance is that the names are approved, but some of them are only of local use. For instance the "common malaria mosquito" is *A. quadrimaculatus*.

Charles Wilcocks

DUBIN, I. N., REESE, J. D. & SEAMANS, Lois A. **Attempt to produce Protection against Mosquitoes by Active Immunization.** *J. Immunology.* 1948, Mar., v. 58, No. 3, 293–7. [13 refs.]

"In this experiment the attempt to protect rabbits against mosquitoes by vaccination with mosquito antigen proved unsuccessful. Moreover, the rabbits so inoculated with a crude suspension of mosquitoes became sensitized to mosquito bites in contrast to the normal non-sensitive rabbits. The sensitized rabbits showed large indurated reddened papules at the site of the bites. These cutaneous reactions began in about 30 minutes and reached their maximum size at about 5 hours.

"Attempts at desensitization of the sensitive animals were unsuccessful under conditions of the present experiment. Passive transfer of the sensitivity to normal animals was also tried but without success."

FLOCH, H. & ABONNENC, E. Sur *Anopheles nunez-tovari* et *A. pessoai* en Guyane française. Table d'identification des *Nyssorhynchus* guyanais. [*Anopheles nunez-tovari* **and** *A. pessôai* **in French Guiana. Key to the** *Nyssorhynchus* **of Guiana.** *Bull. Soc. Path. Exot.* 1947, v. 40, Nos. 11/12, 457–62.

MOSQUITO CONTROL. Suva, Fiji. Revised 1947. 43 pp., 39 figs. [11 refs.] **Training Manual, including Section on the Organization of the Filariasis Campaign in Fiji** [AMOS, D. W., Senior Mosquito Inspector].

This short pamphlet was written by a retired successful business man who became a Mosquito Inspector when manpower was short during the war, and who developed great interest in, and aptitude for, entomological work. It is written as a guide for field inspectors; the language is simple and clear, and there are many excellent line drawings of mosquito larvae and adults showing the important anatomical features. The mosquitoes concerned are those found in Fiji.

The pamphlet includes a key for the identification of larvae, notes on adults and their habits (various species of *Aëdes*, *Culex* and others are described) a section on mosquitoes as vectors of disease, and a section on filariasis in which the author gives his views on methods of control.

The author has studied his material at first hand, and has consulted recognized authorities. The pamphlet will undoubtedly be useful, and, indeed, has already proved its value; the comments of Dr. McGusty and Dr. Buchanan in their forewords leave no doubt on that point. *Charles Wilcocks*

FLOCH, H. & ABONNENC, E. Phlébotomes de la Guyane française (XXII). Clef d'identification de 144 phlébotomes mâles du nouveau continent. [**The** *Phlebotomus* **of French Guiana. (XXII). Key to 144 Male** *Phlebotomus* **of the Americas.**] *Institut Pasteur de la Guyane et du Territoire de l'Inini. Publication No. 161.* 1947, Sept., 17 pp.

SMITH, C. N. & GOUCK, H. K. **The Control of Chiggers in Woodland Plots.** *J. Econom. Entom.* 1947, Dec., v. 40, No. 6, 790–95.

JAYEWICKREME, S. H. & NILES, W. J. **Rearing of** *Trombicula acuscutellaris* **Walch.** *Nature.* 1947, Oct. 25, 578.

The authors describe, with much useful detail, the method by which they have reared four generations of this mite.

They generally feed nymphs or adults on eggs of mosquitoes, but have seen them feed on small freshly-killed insects of several sorts. Eggs are laid in damp cellulose wadding. They hatch in ten to twelve days. The larvae are fed on white mice, which must be immobilized until the larvae have attached themselves. The engorged larvae drop off from the third to the seventh day. [See also this *Bulletin*, 1946, v. 43, 1079.] *P. A. Buxton*

KOHLS, G. M. *Ixodes radfordi*, **a New Species of Tick from Rats in Eastern India (Acarina : Ixodidae).** *J. Parasitology.* 1947, Dec., v. 33, No. 6, 497–8, 1 fig.

WISECUP, C. B., WHITE, W. C. & MINNICH, V. S. **Airplane Spraying with DDT for Control of Salt-Marsh Mosquito Larvae.** *Mosquito News.* 1947, Sept., v. 7, No. 3, 103–8.

"Large-scale applications of DDT sprays from airplanes as preflooding treatments gave no control of salt-marsh mosquito larvae in 1945.

"Direct application of DDT sprays by airplanes is a feasible method of controlling salt-marsh mosquito larvae. The treatments must be applied before pupation commences, and sufficient material should be applied so that it penetrates the vegetative cover. A minimum effective dosage was 0·2 pound of DDT per acre. More satisfactory control was secured from the application of 0·4 pound of DDT per acre. At this dosage a sufficient amount of DDT to control *Aedes* larvae penetrated all except the tallest and densest vegetation."

BIRT, D. H. **D.D.T. in S.E.A.C.** *J. Roy. Nav. Med. Serv.* 1947, July, v. 33, No. 3, 197–200, 1 chart.

GUNTHER, F. A. **Thermal Decomposition of DDT and Benzene Hexachloride Mixtures.** *J. Econom. Entom.* 1947, Dec., v. 40, No. 6, 874–7. [10 refs.]

"Thus it becomes apparent that benzene hexachloride in any of the forms studied has a pronounced deleterious effect upon the thermal stability of DDT in admixture. In all probability the hexachloride preparations contained minute traces of iron or other catalyzing materials which elicited this response. Benzene hexachloride and its alpha, beta, gamma, and delta isomers appear to be quite stable thermally to 120°C. even with added ferric iron, in contradistinction to the behavior of DDT under similar experimental conditions."

REPORTS, SURVEYS AND MISCELLANEOUS PAPERS

CONGO BELGE. Rapport sur l'Hygiène Publique au Congo Belge pendant l'année 1946. [**Report on the Public Health in the Belgian Congo during 1946.**] [LAMBRICHTS, G. P.] 202 mimeographed pp., 2 charts & 2 folding maps.

This report, in addition to covering the medical activities of the Belgian Congo during the year 1946, contains some observations relating to 1945, as publication of the report for the latter year was delayed.

Staff shortage was acute during 1946, since as many members as possible were allowed to take post-war leave, and replacements were difficult to obtain. The report contains the usual detailed statistical account of the work of government, missionary and philanthropic bodies. Comprehensive figures are given for the incidence of the common infectious diseases, and for attendances, treatments and epidemiological data. In many cases, comparative figures are given for the preceding ten to fifteen years.

The report contains a vast amount of informative matter, and gives a very full indication of the extent and nature of the medical problems encountered and of the facilities available for dealing with them.

H. J. O'D. Burke-Gaffney

BULL. INST. HYG. MAROC. 1945, v. 5, 97–189, 9 charts. Rapport sur l'activité des Services de la Direction de la Santé Publique et de la Famille pendant l'année 1945. [**Public Health Activities during 1945 in Morocco.**]

The Directorate of Public Health of Morocco encountered special difficulties in 1945. More than half its personnel was engaged on war duties; unprecedented scarcity, due to deficient rain, coincided with a severe epidemic of relapsing fever which spread from Tunisia and Algeria. There was also an outbreak of typhus fever and small outbreaks of plague in the Casablanca region. Mild smallpox was also prevalent throughout the territory. Malaria, on the other hand, was less prevalent than usual, thanks to deficient rain.

Temporary hospital accommodation had to be created. The total number of hospital admissions was 96,084: "fevers" were responsible for 59·5 per cent. of these admissions. Among these there were 1,520 cases of relapsing fever; 149 typhus fever; 275 smallpox, and malaria 6,510 cases, mostly mild. Malnutrition contributed to high case-mortality rates.

The death rates for the year in the 18 municipalities were Mussulmans 36, Jews 19·8, Europeans 10 per thousand.

Registered cases of smallpox numbered 2,618, of which 36 were among Europeans; vaccinations numbered 1,667,898. Diphtheria prevalence is decreasing; only 203 cases and 16 deaths were recorded. There were 51,975 declared cases of amoebic dysentery and 4,175 cases of bacillary dysentery. These figures give an exaggerated idea of the importance of the outbreak. During 1945, the influx of very large numbers of ill-nourished destitute persons, many of whom were suffering from diarrhoea with blood and mucus, was on such a scale as to preclude the possibility of laboratory investigation in most cases.

Before 1945, no large-scale epidemic of louse-borne relapsing fever had ever been experienced in Morocco. Cases of the African (tick-borne) form of the disease are reported from time to time, chiefly in the region of Port-Lyautey. The Health Service was alive to the dangers of the introduction of epidemic relapsing fever from Algeria, but, unfortunately, adequate supplies of DDT were not available till the end of July, when the epidemic was near its height. The

first cases were recognized in January and the incidence curve rose steadily during the subsequent six months. For the country as a whole the acme of the epidemic was reached in the early weeks of 1946. In any given locality, however, the epidemic was not so long drawn out: it usually reached its height in 3 or 4 months and then rapidly subsided. (By August 1946 the disease had disappeared from Morocco.) During 1945, 26,390 cases of relapsing fever were notified. The case-mortality rate varied from place to place and from season to season, between 1·8 and 8·9 per cent.

Typhus fever notifications were 8,168; the disease was widespread. The case-mortality rate for natives of Morocco, 13·7 per cent., was higher than usual owing to the undernourished condition of the population at risk.

There were 828 cases of plague. *Norman White*

DOCUMENTS ALGÉRIENS. Sér. Soc. 1946, Sept. 15, No. 9, 13 pp. L'oeuvre de l'Institut Pasteur en Algérie [SERGENT, Ed., Director]. [**The Work of the Pasteur Institute in Algeria.**]

A review of work undertaken since 1900.

GUYANE FRANÇAISE. Rapport sur le fonctionnement technique de l'Institut Pasteur de la Guyane Française et du Territoire de l'Inini pendant l'année 1946 [FLOCH, H., Director]. [**Report of the Pasteur Institute of French Guiana and Inini for the Year 1946.**] Publication No. 151. 168 pp. 1947. Cayenne.

The amount of work done by the Director of this Institute, and his assistants, during 1946, was remarkable both for scope and quantity, and in the Report a very detailed account is presented. The tables of pathological and other scientific examinations performed occupy some 20 pages, and include statements of organisms found or cultivated, and of insects and other creatures identified.

In section 4 there are essays, of different lengths, in which current medical problems are discussed—leprosy and its diagnosis and treatment; tuberculosis; venereal diseases; yaws; leishmaniasis; brucellosis; meningitis; beriberi (of which there was an outbreak in 1943); cancer; and other conditions. Malaria is discussed in the following section, and an account is given of a series of investigations on spleen rates (8–60 per cent.), parasite rates (5–46 per cent., *P. falciparum* being by far the most common) and other indices. *Anopheles aquasalis* and *A. darlingi* are the most common anophelines, but only the latter has been found infected in nature, though *A. aquasalis* can be infected experimentally. In this section also there is an account of the preparation of diphtheria anatoxin (Ramon) and its use in a small outbreak, a detailed statement of the leprosy position and the measures taken to deal with it, and statements of the examinations performed in relation to the dysenteries and diseases of the typhoid group.

Examination for intestinal parasites (especially for *Ascaris*, hookworm and *Trichuris*), blood-group work, veterinary work, botanical work and entomological work (reported in great detail) complete this section. The Report concludes with a statement of vaccines, sera, etc., prepared and of vaccinations performed.

The Report is long and detailed, and there is some repetition; but within its limits (as the account of an institute dealing largely with infective or parasitic diseases) it gives a comprehensive picture of conditions in French Guiana.

Charles Wilcocks

Ross, S. G. **Fanning Island (Central Pacific): its Past and Present.** *Med. J. Australia.* 1947, Nov. 1, v. 2, No. 18, 540–48, 14 figs. (1 map). [16 refs.]

Fanning Island is part of the Gilbert and Ellice Islands Colony; it is situated 228 nautical miles north of the equator at 3° 54′ N and 159° 23′ W. It is an atoll, with a large central lagoon. There is a cable station and there are plantations with 140,000 mature coconut palms; these plantations cover 3,122 of the 8,500 acres of land on the island.

The author describes the geological formation and animal life of the island. There are no anophelines, but *Aëdes scutellaris* is found, and sporadic cases of dengue occur; there are no infective diseases. The climate is remarkably even, and the south-east trade wind is cool and almost constant. Rainfall is some 70 inches, and collected rainwater is the drinking water of the inhabitants, of whom there are over 200, mostly labourers who come for a 2-year term. Much of the food is imported.

This is an interesting description of an island of which little is generally known; those who have any dealings with it should read the original.

Charles Wilcocks

BOOK REVIEWS

Gelfand, Michael. [M.B., Ch.B.(Cape Town), M.R.C.P.(Lond.), D.M.R.(Eng.), Government Medical Service, Southern Rhodesia, etc.]. **The Sick African. A Clinical Study.** With a Foreword by A. P. Martin, O.B.E., M.D. Second Revised Edition. 699 pp., 3 coloured diagrams & 121 figs. on pls. 1948. Cape Town: Stewart Printing Co. (Proprietary) Ltd., "Carlton House", Alfred Street. [38s.]

The size of "The Sick African" has been doubled in three years. If this represents as rapidly increasing a concern about him, it is a welcome sign of the times.

Though this book is "a clinical study" the author, who is acting pathologist to the Pasteur Institute as well as physician to the Native Hospital at Salisbury, introduces his observations of an extensive post-mortem room experience. He has also drawn widely on the publications of workers in other parts of Africa and full references are given under chapter headings at the end of the book.

The relative frequency of diseases in Europeans and Africans is a regular feature, stated wherever possible in statistical form, but more often in the customary rather vague phraseology of "not uncommon", "commoner than believed", "relatively rare", etc.

The adoption of the systematic classification rather than the aetiological one necessarily involves a good deal of repetition, but is sound in a clinical treatise.

Despite the comprehensive nature of the work, the author is describing for the most part conditions which he has seen and his observation is wide and his opinions sound. He has made an effort to sort out the tangles of anaemias, nervous diseases and deficiency states as they affect Africans. Occupational diseases such as silicosis also receive due attention, as also does the frequency of cirrhosis of the liver.

It is less a book for the lay worker than for the doctor and, in fact, a hope is expressed that it may be useful for those working for higher degrees in Tropical Medicine.

There is very little to criticize and much to praise. One would perhaps have liked a little stronger warning about the use of carbon tetrachloride. One will look for results of the sulphone drugs in leprosy as they begin to be used in South Africa. A résumé of the use of the antibiotics might be helpful.

There are very few misprints, but there are a few mis-spellings such as "Chrysopsis", "carbasone" for carbarsone, "pharynoderma", and "*S. stercorales*".

The cure of the sick African is rightly stated to lie in the training of African doctors in their own country. But this will take a long time and the economic development of the continent is being so accelerated that less highly trained men may have to be used for generations. Let us hope that a worthy Native Medical School may before long be set up in the Rhodesias.

C. C. Chesterman

MITCHELL, John P. [C.B.E., M.D.]. **Anatomy and Physiology, and Causes of Disease.** 2nd Edition. pp. xvi+226, 87 figs. & 2 diagrams. Baillière's Elementary Tropical Handbooks. 1948. London: Baillière, Tindall & Cox, 7 & 8, Henrietta Street, Covent Garden, W.C.2. [5*s*.]

This is the second edition of one of the Elementary Tropical Handbooks for nurses and orderlies which are becoming as familiar in the tropics as the publisher's "Aids" series are in Britain.

The elementary principles of anatomy and physiology are simply stated and adequately illustrated under headings which correspond with the various systems of the body.

The knowledge thus imparted is reinforced in each chapter by the inclusion of suggestions for a series of simple demonstrations on the living subject, the cadaver or on available animals, etc. The whole is related to clinical and ward work by the introduction of notes on the common diseases of the organs or tissues described.

Thus, theory, demonstration and application go hand in hand throughout the book and the student is kept close to demonstrable facts and familiar realities.

In the pathological section one misses among the various causes of disease any reference to congenital conditions, degenerations and neoplasms (except under unknown causes). The life history of the malaria parasite needs bringing up to date and the rickettsiae might find a humble place between the viruses and the bacteria in view of the prevalence of some sort of typhus fever in so many parts of the tropics.

The author wisely insists in his preface that this book is meant to be used by those who are receiving tuition. All those engaged in teaching will find it an invaluable aid.

The only misspelling noticed was '*Onchocercus*' for '*Onchocerca*' on p. 213 and in the index. This edition contains new sections dealing with blood pressure, shock and blood transfusion. Otherwise only minor changes have been made in the revised text.

C. C. Chesterman

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